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13. ABSTRACT *(Maximum 200 Words)*

This investigation evaluated the influence of gender and phase of menstrual cycle [follicular (FOL: days 2-6) and luteal (LUT: days 19-24) phases] on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C) in 10 females (22.4 ± 2.8 yrs) and 16 males (22.4 ± 2.9 yrs) and then correlated the thermosensitivity to the change (Δ) in Tes and HP across 90-min of resting exposure during a cold air tolerance test (CATT). In addition, the influence of ethnicity, Caucasian (CAU) vs. African American (AA), on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C) in 15 CAU (22.7 ± 2.7 yr.) vs. 7 AA (21.7 ± 2.7 yr.) males was evaluated as well as the influence of age (18-30 vs. 40-50 yr old). ANOVA revealed no significant difference in thermosensitivity between phases of the menstrual cycle or between men and women (FOL = -2.76, LUT = -3.05, Males = -3.24 $W \cdot kg^{-1} \cdot °C^{-1}$). Therefore, these data indicate that when faced with a cold challenge, women respond similarly to men in both phases of their menstrual cycle. Additionally, there was no relationship found between ß and ΔHP and ΔTes in the males and females. Also, there was no relationship between β and thermoregulation during the CATT in these subjects. These data suggest that menstrual cycle phase did not cause a differential response in Tes, Tsk, and HP during a CATT. Furthermore, women maintained a higher Tes than men during the CATT despite similarities in HP and Tsk. Additionally there was no significant difference in thermosensitivity between CAU and AA (CAU = 3.5± 1.6 vs. AA= 2.4 ± 1.4 $W \cdot kg^{-1} \cdot °C^{-1}$). However, a significant ($p<0.05$) main effect for ethnicity for Tes was observed (CAU = 36.7± 0.1 vs. AA = 36.5± 0.1°C). These data suggest, despite a differential response in Tes between AA and CAU groups, the ß of HP during cold water immersion is similar between CAU and AA. Therefore, these data demonstrate that when faced with a cold challenge, there is a similar response in HP between CAU and AA that is accompanied by a differential response in Tes.

14. SUBJECT TERMS
thermoregulation, gender, ethnicity,cold exposure

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(3) Table of Contents

(3) Table of Contents (continued)

(4) INTRODUCTION

Subject. The present investigation quantifies central thermosensitivity from the selective manipulation of esophageal (Tes) temperature at a constant skin temperature. One of the difficulties in assessing thermosensitivity of metabolic heat production in man is the inability to control for differences in absolute temperatures of both the skin and core thermosensors as well as their rates of cooling, all of which are factors that contribute to the thermogenic response (1). Mittleman and Mekjavic (1,2), however, validated a technique for evaluating central thermosensitivity during cold water immersion. This technique, which controls absolute and dynamic skin temperature by immersion in water, enables the core temperature to be manipulated so that the thermoresponsiveness of all subjects are evaluated at similar absolute and dynamic core temperatures. This unique technique involves the occlusion of extremity blood flow for 10-min to allow limb blood to cool towards the temperature of the surrounding tissues. Upon release of cuff pressure, the cooled trapped blood returns to the core region initiating a decrease in Tes, with a concomitant increase in heat production (HP). The slope of this Tes-HP relationship during the dynamic post-occlusion phase is defined as central thermosensitivity. The authors (1) evaluated thermosensitivity of metabolic HP in European-American males age 23 ± 4 yrs and revealed that the heat production response to a similar skin and core thermal drive was unrelated to body composition and size (3) or aerobic fitness (4). In addition, central thermosensitivity, was correlated to the change (Δ) in Tes and HP across the 90-min of resting exposure during the cold air tolerance test (CATT).

Purpose/Scope: The purpose of this investigation was to therefore determine if central thermosensitivity differs between males and females, or, if menstrual cycle phase age, ethnicity or age would affect central thermosensitivity. In addition, it is uncertain if central thermosensitivity (as determined in water) is correlated to a cold air tolerance test.

(5) BODY

According to the revised SOW that was submitted May 1995, the following objectives were evaluated:

Year 1: The influence of gender and menstrual phase on thermosensitivity during cold water immersion (Note: published manuscript Appendix A).

The influence of gender and menstrual cycle on a cold air tolerance test and its relationship to themosensitivity (Note: published manuscript: Appendix B).

Year 2: The influence of ethnicity on thermosensitivity during cold water immersion

[Note: in press manuscript (Aviation Space and Environmental Medicine): Appendix C].

Year 3: The influence of age on thermosensitivity during cold water immersion.

(Note: publication in review Appendix D).

(6) KEY RESEARCH ACCOMPLISHMENTS:

- Despite gender differences in heat production (HP), the thermosensitivity of HP during cold water immersion is similar between males and females and is not influenced by menstrual cycle phase.
- When faced with a cold challenge, women respond similarly to men in both phases of their menstrual cycle.
- Menstrual cycle phase did not cause a differential response in esophageal temperature (Tes), mean skin temperature (Tsk), and HP during a cold air tolerance test (CATT).
- Women maintained a higher Tes than men during the CATT despite similarities in HP and Tsk.
- Despite a differential response in Tes between African Americans (AA) and Caucasian (CAU) groups, the thermosensitivity of HP during cold water immersion is similar between CAU and AA.
- When faced with a cold challenge, there is a similar response in HP between CAU and AA that is accompanied by a differential response in Tes.
- There was no relationship between β and thermoregulation during the CATT in these protocols.
- Despite a trend towards a difference in heat production (HP), with age the thermosensitivity of HP during cold water immersion is similar between young and old individuals
- When faced with a cold challenge, young and old individuals respond similarly with no difference in Tsk, Tes, HP or β.

(7) REPORTABLE OUTCOMES:

Manuscripts, abstracts, presentations

Manuscripts

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewicz, KD Mittleman (2000) The influence of gender and menstrual phase on thermosensitivity during cold water immersion. Aviation Space and Environmental Medicine71(7)715-722.

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewicz, and T Scharschmidt (2000) The influence of gender and menstrual phase on substrate utilization during cold water immersion. Wilderness and Environmental Medicine 11: 5-11.

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewicz (2000). The relation between a cold air tolerance test and thermosensitivity in males and females. Undersea and Hyperbaric Medicine. 27(2) 75-81.

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewics (In press). The influence of ethnicity on thermosensitivity during cold water immersion. Aviation Space and Environmental Medicine.

Glickman EL, N Caine, CC Cheatham, M Blegen. (In review) The influence of age on thermosensitivity during cold water immersion.

Abstracts/Presentations

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewics (2001). The influence of ethnicity on thermosensitivity during cold water immersion. American College of Sports Medicine 48th Annual Meeting, Baltimore, MD

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewicz (2000). The relation between a cold air tolerance test and thermosensitivity in males and females. American College of Sports Medicine 47th Annual Meeting, Indianapolis, IN.

E Glickman-Weiss, K Mittleman, C Cheatham, N Caine, M Blegen (1999) The influence of gender and menstrual phase on thermosensitivity during cold water immersion. American College of Sports Medicine 46th Annual Meeting, Seattle, WA

Scharschmidt T, E Glickman-Weiss (1999) The effects of gender and menstraual phase on carbohydrate utilization during cold exposure. 108th Annual Meeting of the Ohio Academy of Science, April 24, 1999 Cleveland State University, Cleve, OH.

Employment or research opportunities applied for and/or received on experiences/training supported by this award:

C Cheatham: doctoral student and co-author, obtained a post-doctoral position at the John Pierce Foundation, Yale University beginning January 2001.

T Scharschmidt: undergraduate Honor's student is currently in his second year of Medical Scholl at North East Ohio University College of Medicine.

(8) CONCLUSIONS:

- The thermosensitivity of HP during cold water immersion is similar between males and females and is not influenced by menstrual cycle phase or age.
- When faced with a cold challenge, women respond similarly to men in both phases of their menstrual cycle.
- Menstrual cycle phase did not cause a differential response in esophageal temperature (Tes), mean skin temperature (Tsk), and HP during a cold air tolerance test (CATT).
- Women maintained a higher Tes than men during the CATT despite similarities in HP and Tsk.
- Despite a differential response in Tes between African Americans (AA) and Caucasian (CAU) groups, the thermosensitivity of HP during cold water immersion is similar between CAU and AA.
- When faced with a cold challenge, there is a similar response in HP between CAU and AA that is accompanied by a differential response in Tes.
- When faced with a cold challenge, there is a similar response in HP between old and young individuals that is accompanied by a differential response in Tes.

(9) REFERENCES (from Introduction Section)

1. Mittleman KD, Mekjavic IB. Contribution of core cooling rate to shivering thermogenesis during cold water immersion. Aviat Space and Environ Med 1991; 62: 842-8.

2. Mittleman KD, Mekjavic IB. Effect of occluded venous return on core temperature during cold water immersion. J Appl Physiol 1988; 65: 2709-13.

3. Mittleman KD. Role of morphology on central thermosensitivity of heat production during cold water immersion. The FASEB Journal 1990; 4: A278.

4. Mittleman KD. Effect of aerobic fitness on central thermosensitivity of heat production during cold water immersion. Med Sci Sp Exer 1990; 22: S38.

(10) Appendices

Appendix A.

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewicz, KD Mittleman (2000) The influence of gender and menstrual phase on thermosensitivity during cold water immersion. Aviation Space and Environmental Medicine71(7)715-722.
(pages 12-19)

The Influence of Gender and Menstrual Phase on Thermosensitivity During Cold Water Immersion

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MARK BLEGEN, M.S., JENNIFER MARCINKIEWICZ, PH.D.,
AND KAREN D. MITTLEMAN PH.D.

GLICKMAN-WEISS EL, CHEATHAM CC, CAINE N, BLEGEN M, MARCINKIEWICZ J, MITTLEMAN KD. ***The influence of gender and menstrual phase on thermosensitivity during cold water immersion.*** **Aviat Space Environ Med 2000; 71:715–22.**

Background: This investigation evaluated the influence of gender and phase of menstrual cycle [follicular (FOL: days 2–6) and luteal (LUT: days 19–24) phases] on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C) in 10 females (22.4 ± 2.8 yr) and 16 males (22.4 ± 2.9 yr). ***Methods:*** Following a 20-min baseline period (BASE), subjects were immersed until esophageal temperature (T_{es}) reached 36.5°C or for a maximum pre-occlusion (Pre-OCC) time of 40 min. An arm and thigh cuff were then inflated to 180 and 220 mmHg, respectively, for 10 min (OCC). Following release of the inflated cuffs (Post-OCC), the slope (β) of the relationship between the decrease in T_{es} and the increase in HP was used to quantify thermosensitivity. ***Results:*** ANOVA revealed no significant difference in thermosensitivity between phases of the menstrual cycle or between men and women (FOL = −2.76, LUT = −3.05, Males = $-3.24\ W \cdot kg^{-1} \cdot °C^{-1}$). A significant ($p < 0.05$) main effect for gender for HP, and a significant ($p < 0.05$) main effect for menstrual phase for mean skin temperature (T_{sk}) were observed. ***Conclusions:*** These data suggest, despite gender differences in HP, that the thermosensitivity of HP during cold water immersion is similar between males and females and is not influenced by menstrual cycle phase. Therefore, these data indicate that when faced with a cold challenge, women respond similarly to men in both phases of their menstrual cycle.

Keywords: Cold exposure, gender, core temperature, thermoregulation.

IT IS WELL ESTABLISHED that a combination of factors such as gender, body composition and morphology, age, and ethnicity may influence an individual's response to cold stress (4,5,21,30). Whether the potential alterations in cold responsiveness are a result of the morphological differences between these groups or are due to differences in thermosensitivity are unknown.

McArdle et al. (14) suggests that the differences in thermoregulation between men and women at rest during cold stress at may be due in part to the sensitivity of the thermogenic response. These authors found that women exhibited an attenuated thermosensitivity of heat production (HP), with a declining T_{re}, compared with men during resting cold water immersion. Additionally, Graham et al. (8) reported that men, along with eumennorrheic and amennorheic women, have different responses to cold stress. Mannino and Kaufman (13) also found a greater responsiveness to cold in women who were similar in body composition to the men studied. In contrast to McArdle (14), Anderson and colleagues (1) reported the thresholds for shivering and sweating and the magnitude of the thermoregulatory null zone (i.e., core temperature range over which shivering and sweating are absent) were similar in men and women despite differences in body composition. These authors were able to compare thermoregulatory responses to similar peripheral and core thermal drives during immersion in thermoneutral (28°C) water.

Gonzalez and Blanchard (7) as well as Stephenson and Kolka (25) report that a linkage exists between reproductive hormones and thermoregulation in women. These authors (7) suggest that hormonal levels at each menstrual cycle phase, core temperature, and peripheral inputs must be considered in quantifying thermoregulatory responses in women during cold stress. Gonzalez and Blanchard (7) evaluated the thermoregulatory responses to cold air transients (20 to −5°C at $-0.32°C \cdot min^{-1}$), during the different menstrual cycle phases in resting clothed women (two different military clothing systems). These authors (7) suggest that during transient cold stress in resting women at two stages of the menstrual cycle, a decreased slope in luteal phase was observed when shivering thermogenesis was plotted against integrated body temperature. In addition, during the luteal phase, women demonstrated an increase in cutaneous heat flux, but rate of heat debt was reduced. According to these data, a differential thermoregulatory response was demonstrated that is linked to the individuals varying hormonal status. Based on their review of the literature, Stephenson

From the Kent State University, School of Exercise, Leisure & Sport, Exercise Sciences Laboratory (E. L. Glickman-Weiss, C. C. Cheatham, N. Caine, M. Blegen); Kent State University, Department of Biological Sciences, Kent, OH (J. Marcinkiewicz); and DesignWrite, Princeton, NJ (K. D. Mittleman).

This manuscript was received for review in June 1999. It was revised in October and was accepted for publication in December 1999.

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and Kolka (25) suggest that studies of thermoregulatory effector function during cold exposure over the menstrual cycle are warranted, as it is uncertain if there exists a true differential response between men and women that may be confounded by menstrual cycle phase.

The present investigation quantifies central thermosensitivity from the selective manipulation of esophageal (T_{es}) temperature at a constant skin temperature. This unique technique involves the occlusion of extremity blood flow for 10 min to allow limb blood to cool toward the temperature of the surrounding tissues. On release of cuff pressure, the cooled trapped blood returns to the core region initiating a decrease in T_{es}, with a concomitant increase in heat production (HP). The slope of this T_{es}-HP relationship during the dynamic post-occlusion phase is defined as central thermosensitivity. One of the difficulties in assessing thermosensitivity of metabolic heat production in man is the inability to control for differences in absolute temperatures of both the skin and core thermosensors as well as their rates of cooling, all of which are factors that contribute to the thermogenic response (18). Mittleman and Mekjavic (18,19), however, validated a technique for evaluating central thermosensitivity during cold water immersion. This technique, which controls absolute and dynamic skin temperature by immersion in water, enables the core temperature to be manipulated so that the thermoresponsiveness of all subjects is evaluated at similar absolute and dynamic core temperatures. The authors (18) evaluated thermosensitivity of metabolic heat production in European-American males age 23 ± 4 yr and revealed that the heat production response to a similar skin and core thermal drive was unrelated to body composition and size (17) or aerobic fitness (16). It is uncertain, however, if central thermosensitivity differs between males and females, or, if menstrual cycle phase would affect central thermosensitivity.

Therefore, whether: a) a more severe cold challenge (i.e., temperature of environment, air vs. water environmental challenge, duration of immersion, and seminude condition); b) the examination of gender and menstrual phase; and c) the systematic control of central and peripheral inputs would also result in similar core thermosensitivities in men and women has not been examined and thus renders investigation. The purpose of the present investigation was to evaluate the influence of gender and the phase of the menstrual cycle on thermosensitivity of HP during cold exposure.

METHODS

Subjects

Healthy, active Caucasian men (n = 16) and women (n = 10), age 18–29 yr, volunteered to participate in the study (**Table I**) and provided informed consent. The Institutional Review Board approved all experimental procedures for Human Subjects Research. Subjects completed the cold trials between April and mid-November to limit the potential influence of natural cold acclimatization on physiological responses (2). The women were not using oral contraceptives and were eumenorrheic, with confirmation of the follicular (FOL) or luteal (LUT) phase of the menstrual cycle provided by assessment of their serum estradiol (E_2) and progesterone (P_4) values.

TABLE I. SUBJECT CHARACTERISTICS (M ± SD).

Variable	Male (n = 16)	Female (n = 10)
Age (yr)	22.4 ± 2.9	22.4 ± 2.8
Height (cm)	177.3 ± 7.9	166.4 ± 7.3*
Weight (kg)	77.8 ± 11.5	66.4 ± 12.4*
BSA (m^2)	1.94 ± 0.2	1.74 ± 0.2*
Body fat (%)	10.9 ± 2.9	24.6 ± 5.1*
$\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	46.4 ± 9.2	37.5 ± 13.5

BSA, Body Surface Area; *$p < 0.05$, males vs. females.

Pre-Experimental Testing

During the first visit to the laboratory, anthropometric variables and maximal oxygen uptake ($\dot{V}O_{2max}$) were measured. Height and weight were measured via a stadiometer and a balance beam scale, respectively. Skinfold thickness was measured using standardized procedures and percent body fat was calculated using gender specific equations (10,11). Surface area (A_D) was calculated from height and weight using the formula of Dubois and Dubois (3). Each subject performed a maximal exercise test on a magnetically braked cycle ergometer to determine $\dot{V}O_{2max}$. The protocol consisted of increasing the work rate in a progressive manner until maximal voluntary exhaustion was achieved. The test began at 60 W for males and 40 W for females for 2 min and increased 20 $W \cdot min^{-1}$ thereafter. Oxygen consumption ($\dot{V}O_2$) was measured using an automated open circuit system (MAX-1 CART, Physio-Dyne Instrument Company, Quogue, NY). Expired respiratory air samples were collected continuously throughout the maximal exercise test and recorded at 30-s intervals. Heart rate (HR) was recorded every 30 s and rating of perceived exertion (RPE) was assessed during the last 10 s of each exercise stage. $\dot{V}O_{2max}$ was determined to be the average of the two greatest 30 s values.

Water Immersion Protocol

The water immersion protocol consisted of four stages: baseline (BASE), pre-occlusion (Pre-OCC), occlusion (OCC), and post-occlusion (Post-OCC). Subjects were dressed only in shorts (males) or shorts and a jogging bra (females).

Throughout the entire water immersion protocol, core (esophageal) temperature (T_{es}), skin temperature, expired respiratory air samples, and HR were continuously measured. T_{es} was measured using a copper-constantan thermocouple encased in an infant feeding tube (Model # 8888-260406, Sherwood Medical, St. Louis, MO). Insertion depth to the level of the heart was determined by sitting stature (15) with adjustments to obtain the highest temperature reading. Skin temperature was evaluated from seven sites (head, tricep, hand, chest, thigh, calf, foot) using copper-constantan thermocouples. Mean weighted skin temperature (T_{sk}) was calculated using the formula of Ramanthan (19). The esophageal and

TABLE II. CONCENTRATION LEVELS OF ESTRADIOL AND PROGESTERONE DURING BASAL REST PERIODS (M ± SD).

Hormone/Menstrual Phase	Follicular (Days 2–6)	Luteal (Days 19–23)
Estradiol ($pg \cdot mL^{-1}$)	32.94 ± 7.09	111.40 ± 60.63*
Progesterone ($ng \cdot mL^{-1}$)	0.72 ± 0.30	10.61 ± 4.80*

*$p < 0.05$, FOL vs. LUT.

skin temperature thermocouples were interfaced to a datalogger (Omega OM-5000 Data Logger, Omega Engineering, Inc., Stamford, CT) and values were recorded every minute. Expired respiratory air samples were collected and analyzed every minute and used to calculate HP ($W \cdot m^{-2}$). HR was recorded every minute.

During BASE, each subject sat quietly in a semi-recumbent position on a lounge chair for 20 min in 28°C air. Following BASE, 15 cc of blood was drawn from an antecubital vein for the assessment of serum E_2 and P_4 levels.

Immediately following the blood sampling, each subject was escorted to the immersion tank to begin the Pre-OCC stage of the water immersion protocol. Each subject sat immersed to the first thoracic vertebrae with limbs separated and extended on a specially designed chair constructed of PVC tubing. Water temperature of the tank was maintained at 20° (±0.1°C) via a commercially available chiller (Bath Cooler PBC-2II, NESLAB Instrument Company, Newington, NH). After 40 min, or when T_{es} reached 36.5°C, the OCC stage was initiated. BP cuffs around the right arm and left leg were inflated to 180 and 220 mmHg, respectively (18,19). After 10 min of blood occlusion, the cuffs were released and the subject remained in the tank for 10 min (Post-OCC) or until a T_{es} of 35°C. On release of the cuffs, T_{es} decreases resulting from the return of the cooled extremity blood to the core region and HP concomitantly increases. The slope of the stimulus (decrease in T_{es})–response (increase in HP) relationship during the Post-OCC phase was used to define thermosensitivity (β, $W \cdot kg^{-1} \cdot °C^{-1}$). Following the Post-OCC stage, subjects were removed from the immersion tank and escorted to a warm shower for rewarming.

Blood Analyses

Venous blood samples were centrifuged for 10 min at 3000 rpm (IEC Centra-7R, International Equipment Company, Needham Heights, MA) after which the serum was removed and frozen at −70°C for later analysis. Phase of the menstrual cycle was confirmed by measuring serum E_2 and P_4 (**Table II**). Both steroids were analyzed without extraction using a radioimmunoassay kit (Coat-A-Count, Diagnostic Products Corporation, Los Angeles, CA). All analyses for each steroid were determined in a single assay with an average coefficient of variation of 5.88%. Assays were highly specific, with no clinically significant cross-reaction to other steroids or therapeutic drugs that may be present in subject samples.

Statistical Analyses

Data were evaluated for differences between menstrual phase, gender, and across time using analysis of variance (ANOVA) procedures. A two-way (phase × time; 2 × 4) ANOVA with repeated measures on both factors was used to compare the responses during the menstrual phases. If no significant differences were present between menstrual phases, the menstrual phase data was pooled into one data set to be representative of the female responses and a two-way (gender × time, 2 × 4) ANOVA with repeated measures on the time factor was used to analyze gender differences. If there was a significant difference between menstrual phases, a two-way (male, FOL, LUT vs. time, 3 × 4) ANOVA with repeated measures on the time factor was used to determine gender differences. Significance was set a priori at $p < 0.05$. When significance was observed, a Tukey post-hoc test was used to examine specific contrasts. A priori contrasts on the physiological responses at baseline were compared using a Tukey post-hoc test. All values are expressed as means (M) ± standard deviations (SD). HP was analyzed and is expressed as $W \cdot kg^{-1}$ and $W \cdot m^{-2}$ and β was analyzed and is reported as both $W \cdot kg^{-1} \cdot °C^{-1}$ and $W \cdot m^{-2} \cdot °C^{-1}$. Both units of measurement are presented so as to make comparisons with the available experimental literature. Lastly, due to the unequal group sizes, Levene's Test for Equality of Variances was used to determine whether group variances were unequal. If the groups exhibited different variances, an adjusted p-value was used.

RESULTS

Physiological Responses During Baseline

HP was not significantly different between the FOL and LUT phase of the menstrual cycle whether expressed relative to body weight or A_D. However, males exhibited a significantly greater HP when compared with females when HP was expressed relative to A_D (53.42 ± 7.87 and 46.95 ± 6.18 $W \cdot m^{-2}$, respectively). There was no significant difference in HP between males and females when HP was expressed relative to body weight.

There were no significant differences observed in T_{es} between the FOL and LUT phases of the menstrual cycle or between males and females.

T_{sk} was significantly higher in the LUT phase compared with the FOL phase of the menstrual cycle (32.1 ± 0.9 and 31.4 ± 0.6°C, respectively). However, no significant difference in T_{sk} was observed between males and females irrespective of the menstrual phase.

Physiological Responses During Cold Water Immersions

Heat production (HP): HP did not demonstrate a main effect for menstrual cycle phase (FOL vs. LUT), thus, an ANOVA was performed comparing gender (males vs. females pooling cycle phase as one group) which demonstrated a significant main effect for gender ($p = 0.05$) when expressing HP in terms of $W \cdot m^{-2}$ (**Fig. 1**). However, when HP was expressed in $W \cdot kg^{-1}$ there was no main effect for gender demonstrated ($p = 0.16$).

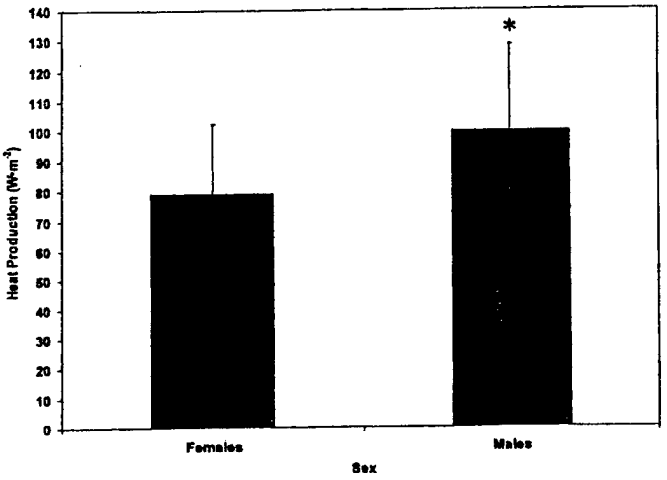

Fig. 1. Comparison of values for heat production (M ± SD): males vs. females, * $p < 0.05$.

A significant main effect for time ($p = 0.001$) was observed (when HP was expressed in either $W \cdot kg^{-1}$ or $W \cdot m^{-2}$) whereby HP exhibited a characteristic elevation during the onset of immersion followed by a slight decrease or plateau during the Pre-OCC and OCC stages and then an increase during the Post-OCC stage (**Fig. 2**). Specifically, post-hoc analysis revealed significant differences between all time periods except for Pre-OCC and OCC (**Table III**). During the Post-OCC stage, increased bursts of shivering were observed.

Esophageal temperature (T_{es}): T_{es} did not demonstrate a main effect for menstrual cycle phase (FOL vs. LUT, $p = 0.29$), thus, an ANOVA was performed comparing gender (males vs. females pooling cycle phase as one group). This analysis also revealed no significant difference ($p = 0.82$) between gender. However, as expected, a significant main effect for time was observed ($p = 0.001$) (**Fig. 3**). Post-hoc testing revealed significant differences between all time periods except for BASE and Pre-OCC (Table III). Additionally, there was no significant group × time interaction demonstrated.

Mean skin temperature (T_{sk}): T_{sk} (pooled across time and group) demonstrated a main effect for menstrual cycle phase; T_{sk}-FOL was lower ($p = 0.04$) than T_{sk}-LUT (**Fig. 4**). However, there was no significant difference in T_{sk} observed when males were compared with females in either phase of the menstrual cycle ($p = 0.18$). **Fig. 5** displays the response in T_{sk} over time. As expected, a significant main effect for time ($p = 0.001$) was observed and subsequent post-hoc testing revealed that the main effect may be attributed to the difference between the BASE and the other time periods as T_{sk} remained unchanged once the cold water immersion began (Table III).

*Central thermosensitivity (β):*The relationship between the decrease in T_{es} and increase in HP following the release of occlusion and subsequent recirculation of the cooled extremity blood is depicted for all subjects in **Fig. 6**. All values for β are given as absolutes. Although there is no significant main effect for group, β was lower in the FOL phase than the LUT phase (2.76 ± 1.30 and 3.05 ± 1.75 $W \cdot kg^{-1} \cdot °C^{-1}$, or, expressed relative to body surface area, 74.47 ± 36.46 and 98.94 ± 53.24, $W \cdot m^{-2} \cdot °C^{-1}$, respectively) which was also lower than the value of β found in the males (3.23 ± 1.72 $W \cdot kg^{-1} \cdot °C^{-1}$ or 115.0 ± 67.0 $W \cdot m^{-2} \cdot °C^{-1}$).

DISCUSSION

In the present study, thermal and metabolic responses were evaluated during immersion in 20°C water following the alteration in blood circulation (by

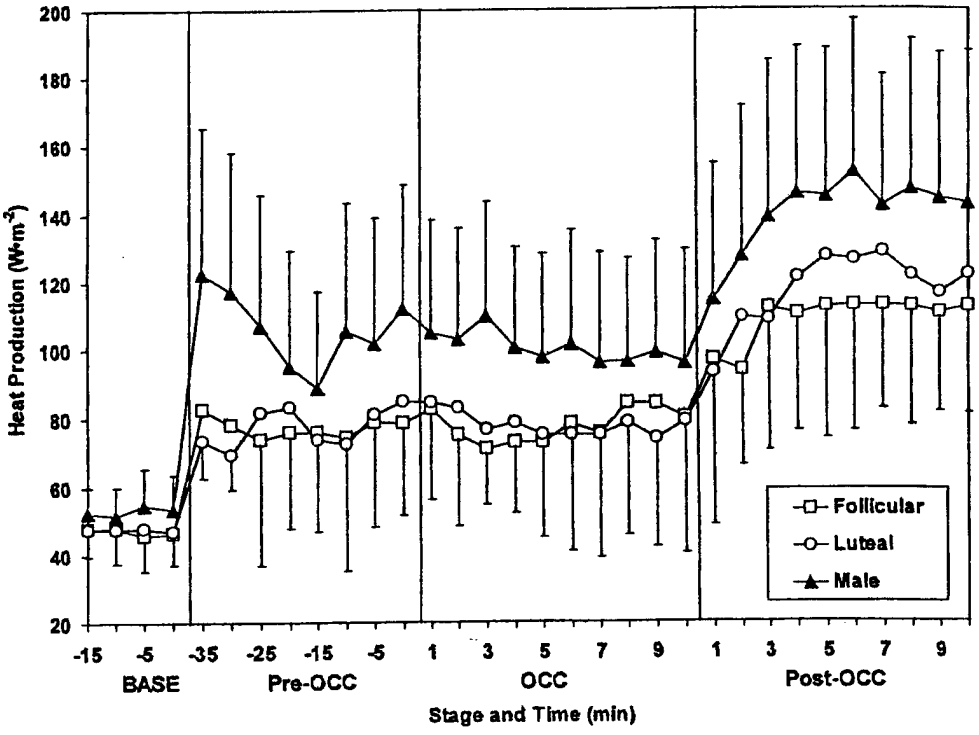

Fig. 2. Mean values for heat production (M ± SD) during baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow.

TABLE III. ESOPHAGEAL TEMPERATURE (T_{ES}), MEAN SKIN TEMPERATURE (T_{SK}), AND HEAT PRODUCTION (HP) ACROSS TIME (M ± SD).

	T_{es} (°C)				$\bar{T}_{sk}$ (°C)				HP ($W \cdot m^{-2}$)			
Stage	FOL	LUT	Male	Total	FOL	LUT	Male	Total	FOL	LUT	Male	Total
BASE	36.9 ± 0.2	37.0 ± 0.3	37.0 ± 0.2	37.0 ± 0.2	31.4 ± 0.6	32.1 ± 0.9	31.7 ± 0.8	31.7 ± 0.8	47.1 ± 8.2	46.8 ± 4.9	53.4 ± 7.9	49.8 ± 7.8
PRE-OCC	36.9 ± 0.3	37.0 ± 0.3	36.9 ± 0.2	36.9 ± 0.3	21.6 ± 0.8	22.1 ± 0.6	22.0 ± 1.0	21.9 ± 0.8	78.3 ± 28.8	78.4 ± 27.9	105.6 ± 35.5	90.5 ± 33.8
OCC	36.7 ± 0.4	36.7 ± 0.4	36.7 ± 0.2	36.7 ± 0.3	21.4 ± 0.7	21.9 ± 0.7	21.6 ± 0.9	21.6 ± 0.8	77.6 ± 26.2	77.9 ± 32.0	100.3 ± 29.4	87.8 ± 30.7
POST-OCC	36.4 ± 0.4	36.4 ± 0.5	36.3 ± 0.3	36.4 ± 0.3	21.5 ± 0.9	21.7 ± 0.5	21.5 ± 0.9	21.6 ± 0.8	108.4 ± 31.7	117.3 ± 38.4	139.9 ± 42.2	124.8 ± 40.0

FOL, Follicular; LUT, Luteal; BASE, Baseline; PRE-OCC, Pre-occlusion; OCC, occlusion; POST-OCC, post-occlusion.

pressure cuff occlusion). The experimental manipulation of T_{es} by pressure cuff occlusion and the subsequent release of the cooled trapped extremity blood, resulted in an increase in shivering thermogenesis and a reduction in T_{es}. This has been reported previously (18,19). In addition, the slope of the T_{es}-HP relationship during the dynamic post-occlusion phase that defines central thermosensitivity did not significantly differ by gender or menstrual cycle phase. This lack of significant difference may be explained by the large variability in the data, indicating that there is a large amount of inter-individual variation in thermosensitivity. The variability in thermosensitivity was similar to that observed in previous studies (18). This study extends the work of Mittleman and Mekjavic (18,19) using a sample of males and females, as well as making comparisons between menstrual cycle phase in an effort to discern if gender and menstrual cycle phase contribute to thermosensitivity as others (7,8,14) have proposed. Values for central thermosensitivity in the present investigation were similar to those previously reported by Mittleman et al. (20) (males: 4.45 ± 0.55 $W \cdot kg^{-1} \cdot °C^{-1}$; females-FOL: 3.38 $W \cdot kg^{-1} \cdot °C^{-1}$; females-LUT: 4.26 ± 0.56 $W \cdot kg^{-1} \cdot °C^{-1}$). Furthermore, these data did not demonstrate a significant differential response between gender or menstrual cycle phase.

Although the present investigation did find a difference between T_{sk} during the FOL and the LUT phase, this differential response was unaccompanied by differences in T_{es}, HP and β. This finding is consistent with others that have reported that T_{sk} is higher in the LUT compared with the FOL phase (9,12,25) of the menstrual cycle. Overall, HP was higher in males compared with females which is consistent with others (14). Since women generally possess greater levels of total body fat and thicker layers of subcutaneous fat than males for any particular body composition, it is not surprising that females should be better able to maintain core temperature with an attenuated metabolic rate com-

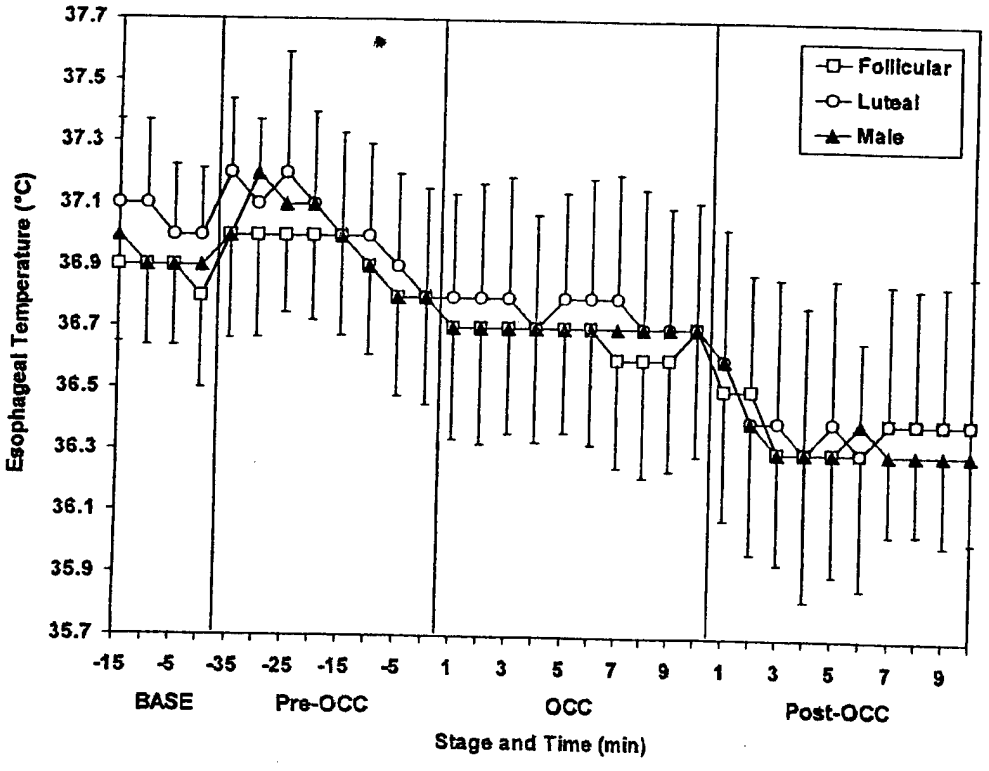

Fig. 3. Mean values for esophageal temperature (M ± SD) during baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow.

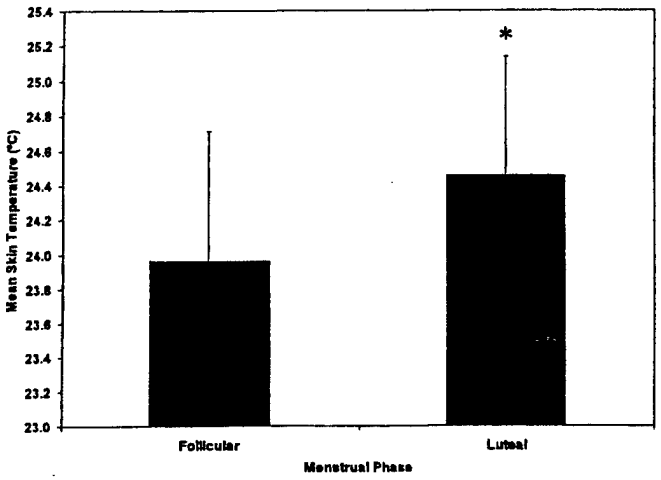

Fig. 4. Comparison of values for mean skin temperature (M ± SD) follicular vs. luteal phase, * $p < 0.05$.

pared with their male counterparts during acute cold exposure.

Gonzalez and Blanchard (7) concluded that endogenous hormonal levels vary between menstrual cycle phase and must be considered in quantifying thermoregulatory responses in women during cold stress. However, they (7) evaluated six clothed women in each of two ensembles with different thermal resistances during both the luteal and follicular menstrual cycle phases. In all conditions the subjects wore light-duty work gloves with a woolen inserts, as well as standard-issue military army boots and socks. In any case, the subjects were all clothed, not semi-nude, and were cold exposed to air temperature transients after a baseline period (15 min in 20°C air). Therefore, it is perhaps the environmental medium, (i.e., cold air vs. cold water), coupled with the exposure to cold air transients as opposed to cold water immersion for a more protracted period of time as well as the clothing ensembles that provided an additional and varying type of insulative component that may have contributed to the differences in the experimental findings. In addition, the protocol employed in the present investigation evaluates the thermogenic response of individuals with similar combinations of core and peripheral inputs during acute cold water immersion. Gonzalez and Blanchard (7) suggest that as long as T_{es} remains near thermoneutral levels, the summed effect of shivering thermogenesis is highly correlated with a combined effect of T_{sk} and temperature of the cold acral area. Since the present investigation did not attempt to maintain T_{es} near thermoneutral levels, the conclusions reached by Gonzalez and Blanchard (7) may not be relevant when attempting to make comparisons to the present investigation. One of the major differences between the present investigation and that of Gonzalez and Blanchard (7) is the core and peripheral inputs. The present investigation attempted to provide similar inputs by clamping skin to water temperature and providing a similar thermal strain at either 40 min of exposure or until T_{es} declined to 36.5°C. In doing so, the present investigation demonstrated a selective manipulation of T_{es} at a constant T_{sk}. Gonzalez and Blanchard (7) suggest that there is extensive interaction (and possible competition) between thermal inputs from skin and deep body receptors that probably temper the final shivering response in women as a function of the menstrual cycle. Thus, the present investigation differs from the Gonzalez and Blanchard (7) study in that the core and peripheral inputs, and thereby the thermal strain, differed. Hessemer and Bruck (9) also evaluated external heat and cold

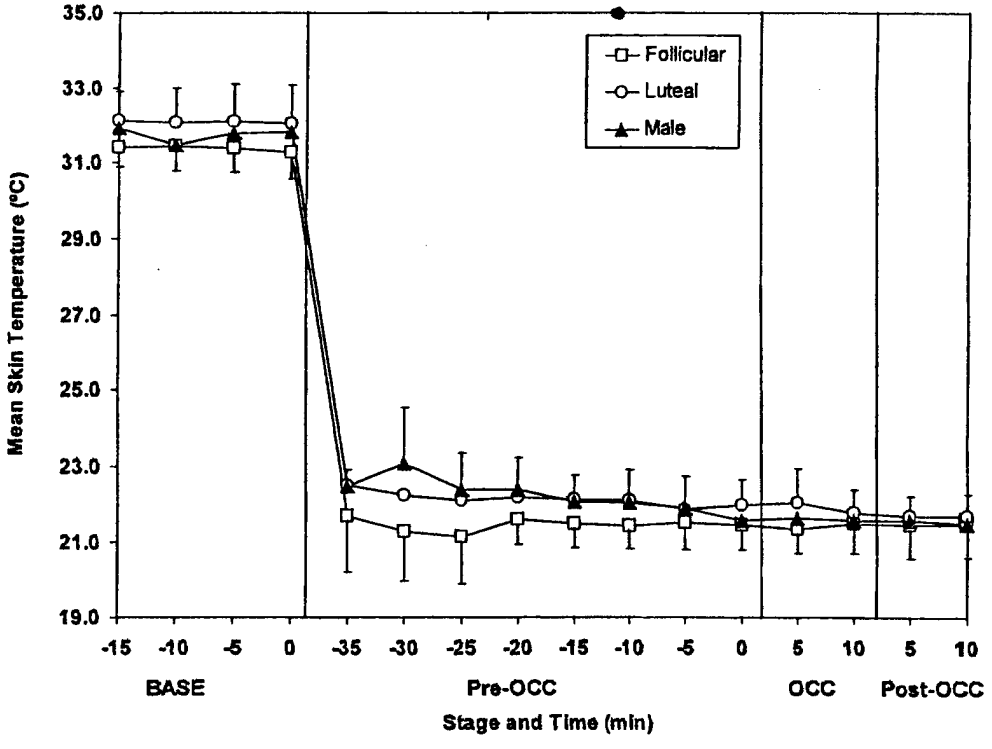

Fig. 5. Mean values for mean skin temperature (M ± SD) during baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow.

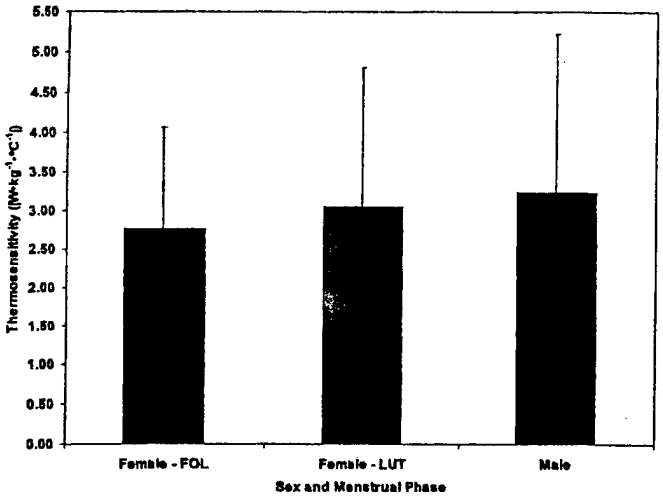

Fig. 6. Comparison of values for thermosensitivity (M ± SD) between females during the follicular phase (Female-FOL), females during the luteal phase (Female-LUT) and males (Male).

exposures in 10 women in the middle of LUT phase and in the early FOL phase of the menstrual cycle. At neutral ambient temperature, T_{es} averaged 0.59°C higher in LUT than FOL. The thresholds for shivering, chest sweating and cutaneous vasodilation at the thumb and forearm were also increased in LUT by an average of 0.47°C, and were related to mean body temperature. The metabolic rate, arm blood flow, and HR at the thermoneutral conditions were also increased in LUT. According to the authors (9), these data collected in hot and cold ambients support the concept of a central resetting of the set point of the thermoregulatory system in the LUT phase. Differences in the cold medium (air vs. water), as well as differences in the thermal drive (absolute and rates of change in core and skin temperatures), may contribute to these equivocal results.

Tikuisis (27,28,29) and Stolwijk and Hardy (24) have shown that shivering thermogenesis is closely linked to thermal signals from the body core and T_{sk} sites and heavily influenced by percent body fat. The peripheral signal in the present investigation as measured via T_{sk} may have differed (FOL vs. LUT) in the present investigation (Fig. 5), however, T_{es} did not differ and was maintained via an attenuated HP for the females compared with the males. This relationship is consistent with the literature as HP is typically higher in leaner individuals than in counterparts with more fat (4) and is typically higher in males than females (13,30) in an attempt to maintain core temperature.

However, because the central measure of thermosensitivity produces similar thermal stressors for individuals that may differ morphologically (i.e., males and females), and evaluates the relationship of the decline in T_{es} to a controlled elevation in HP, the relative involvement of body composition is not a determinant (16). Since the present investigation found that T_{sk} did not differ between males and females, but rather only differed when the data was pooled across FOL vs. LUT phases, the thermal stressor between gender (i.e., groups that differ morphologically) was similar. Thus, for a similar thermal stressor, the variable β, a marker of change in HP which relates to the change in T_{es}, has been shown not to differ between males and females or between menstrual cycle phase.

Further, it is likely that the thermal strain may account for differences between experimental findings and possibly may have masked any thermogenic response between the FOL vs. the LUT menstrual phase or even between gender. Since conductive heat loss in water is 25 times greater than in air, body heat is lost two to four times as fast in cool water as in air at the same temperature (25). However, the lack of significant difference in T_{es}, and β between the males and females, as well as during the FOL vs. the LUT phases, is in partial agreement with Anderson et al. (1) when reporting that men and women respond to deviations in core temperature in a similar manner.

Based on the present findings, more work is needed to discern if the measure of thermosensitivity relates to prediction times of survival during acute cold exposure. Inclusion of individual thermosensitivity of HP has been proposed to improve the prediction of the metabolic response to cold (23–25). Tikuisis (27,28) incorporated body composition as well as individual set point values to enhance the prediction of physiological responses during cold water immersion as well as to predict survival time during cold exposure. Therefore, subsequent work may consider evaluating the individual thermosensitivity between genders and between the menstrual cycle in the prediction of cold responses and survival. Additionally, perhaps the evaluation of substrate utilization, which may possibly differ between gender, and the possible interplay of potential gender based differences in catecholamines and other biochemistries, may further our understanding of gender and menstrual phase differences in thermoregulation.

The determination of central thermosensitivity allows for the assessment of group differences (males vs. females; FOL vs. LUT) in the physiological responses to a decrease in core temperature regardless of the anthropometrical or morphological differences usually expected between these groups (males vs. females). Therefore, the determination of central thermosensitivity may reveal whether or not a certain group of individuals is at a marked disadvantage during cold exposure. If a marked disadvantage is observed, this information could lead to alterations in acceptable exposure time, equipment/insulation needs, and in general guidelines set forth to protect the individual from cold related injuries.

In conclusion, these data suggest that the thermosensitivity of HP during cold water immersion is similar between males and females and is not influenced by menstrual cycle phase.

ACKNOWLEDGMENTS

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Appendix B.

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewicz (2000). The influence of gender and menstrual cycle on a cold air tolerance test and its relation to thermosensitivity. Undersea and Hyperbaric Medicine. 27(2) 75-81.
(pages 21-27)

Influence of gender and menstrual cycle on a cold air tolerance test and its relationship to thermosensitivity

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Glickman-Weiss EL, Cheatham CC, Caine N, Blegen M, Marcinkiewicz J. Influence of gender and menstrual cycle on a cold air tolerance test and its relationship to thermosensitivity. Undersea Hyper Med 2000; 27(2):75–81.—This investigation evaluated the influence of gender and phase of menstrual cycle [follicular (FOL): Days 2–6) and luteal (LUT: Days 19–24)] on a cold air tolerance test (CATT: 90-min of exposure to 5°C air) in 8 females (22.7 ± 3.0 yr) and 15 males (22.3 ± 2.9 yr). In addition, central thermosensitivity (ß; $W \cdot kg^{-1} \cdot °C^{-1}$) [i.e., the slope of the relationship between the decrease in esophageal temperature (T_{es}) and the increase in heat production (HP)], gathered during a separate water trial in 20°C water, was correlated to the change (Δ) in T_{es} and HP across the 90 min of resting exposure during the CATT. Analysis of variance revealed no significant differences between phase of menstrual cycle or gender for HP, mean skin temperature (T_{sk}), and insulation; however, a main effect for time for these parameters was demonstrated. Despite these similarities, T_{es} differed ($P < 0.05$) between males and females. Additionally, no relationship was found between β and ΔHP and ΔT_{es} in the males and females. Also, there was no relationship between β and thermoregulation during the CATT in these subjects. These data suggest that menstrual cycle phase did not cause a differential response in T_{es}, $\overline{T}_{sk}$, and HP during a CATT. Furthermore, women maintained a higher T_{es} than men during the CATT despite similarities in HP and $\overline{T}_{sk}$.

gender differences, thermoregulation, core temperature, metabolism, heat production

It is well established that a variety of factors may influence the individual's ability to regulate to the stressor of cold, which may lead to gender differences in thermoregulation. McArdle and colleagues (1) suggest that the differences in thermoregulation between males and females during cold stress may be due to the sensitivity of the thermogenic response. They (1) reported that females exhibited an attenuated increase in heat production (HP) (with a declining rectal temperature) compared with men during resting cold water immersion. Therefore, it is believed that the evaluation of thermosensitivity (β) between gender and over menstrual cycle may provide important information regarding cold responsiveness. Furthermore, the determination of thermoresponsiveness or thermosensitivity's relationship to the physiologic responses demonstrated during protracted cold exposure renders investigation.

Gonzalez and Blanchard (2) and Stephenson and Kolka (3) report that a linkage exists between reproductive hormones and thermoregulation in women. Core temperature has been shown to be approximately 0.4°C higher in the luteal (LUT) phase than during the follicular (FOL) phase (4). Thermoregulation depends on the balance between heat gained via HP and heat lost to the environment. Furthermore, since HP is influenced by size, body composition (5–7) (i.e., training, surface area to body mass ratio, or body mass), age (1,3), gender (1,3,8), training state (3,7,8), and endocrine function (9), the interplay between the increase in HP and decline in core temperature between genders remains poorly understood.

Thermosensitivity is determined by the selective manipulation of esophageal temperature (T_{es}) at a constant skin temperature (T_{sk}). This technique is unique in that it controls T_{sk} by immersion in water and enables the core temperature to be manipulated so that the thermoresponsiveness of all subjects is evaluated at a similar rate of decline in core temperature. The similar rate of decline in core temperature is accomplished by the occlusion of extremity blood flow for 10 min to allow limb blood to cool toward the temperature of the surrounding tissues. Upon release of cuff pressure, the cooled, trapped blood returns to the core region initiating a decrease in T_{es} with a concomitant increase in HP. The slope of this T_{es}–HP relationship during the dynamic post-occlusion phase is defined as β (10–12).

The purpose of this investigation was to determine if

there are differences in thermal and metabolic parameters between gender and within the female subjects between menstrual cycle phase during prolonged exposure to 5°C air (cold air tolerance test: CATT), and whether the thermoresponsiveness observed during a controlled thermal challenge (20°C water) was related to the responses observed during a 5°C air exposure trial in males and females 18–30 yr of age.

METHODS

Subjects and design: Healthy, active Caucasian males (n = 15) and females (n = 8), age 18–30 yr, volunteered to participate in the study (Table 1) and provided informed consent. The Institutional Review Board approved all experimental procedures for Human Subjects Research. Subjects completed the cold trials between April and mid-November to limit the potential influence of natural cold acclimatization on physiologic responses (13). In addition, all trials were conducted at the same time of day for each subject. Each subject reported to the laboratory on separate days for pre-experimental testing, a CATT, and a cold water immersion trial (CWT). Subjects were instructed to refrain from eating, physical activity, caffeine, and alcohol for the 12 h preceding each trial. For female subjects, the CATT and the CWT were completed in both the FOL (Days 2–6) and LUT (Days 19–24) phases of the menstrual cycle. The females were not using oral contraceptives and were eumenorrheic, with confirmation of FOL or LUT phase of the menstrual cycle provided by assessment of their serum estradiol (E_2) and progesterone (P_4) values.

Pre-experimental testing: During the first visit to the laboratory, anthropometric variables and maximal oxygen uptake ($\dot{V}O_{2max}$) were measured. Height and weight were measured via a stadiometer and a balance beam scale, respectively. Skinfold thickness was measured using standardized procedures, and percent fat was derived via body density using gender specific equations (14,15). Surface area (A_D) was calculated from height and weight using the formula of Dubois and Dubois (16). Each subject performed a maximal exercise test on a magnetically braked cycle ergometer to determine $\dot{V}O_{2max}$. The protocol consisted of increasing the work rate in a progressive manner until volitional exhaustion was achieved. The test began at 60 W for males and 40 W for females for 2 min and increased 20 W · min^{-1} thereafter. Expired air samples were collected continuously throughout the maximal exercise test and analyzed for oxygen and carbon dioxide concentrations using an automated open circuit system (MAX-1 CART, Physio-Dyne Instrument Company, Quogue, NY). Heart rate was recorded every 30 s via telemetry (Polar USA, Port Washington, NY) and rate of perceived exertion (RPE) was assessed during the last 10 s of each exercise stage. $\dot{V}O_{2max}$ was determined to be the average of the two greatest 30-s $\dot{V}O_2$ values recorded during the test.

Cold air tolerance test: The CATT consisted of a baseline period (BASE) and a cold air exposure period (AIR). Subjects were dressed only in shorts (males) or shorts and an athletic bra (females).

Before the beginning of BASE, 15 ml of blood was drawn from an antecubital vein for the assessment of serum E_2 and P_4 levels in female subjects only. During BASE, each subject sat quietly in a semi-recumbent position on a lounge chair for 30 min in 23°–26°C air. Immediately following BASE, each subject was escorted to the environmental chamber to begin the AIR stage of the CATT. Each subject sat quietly in a semi-recumbent position on a lounge chair for 90 min in 5°C air.

Throughout the entire CATT, T_{es}, T_{sk}, expired air samples, and heart rate were continuously measured. T_{es} was measured using a copper-constantan thermocouple encased in an infant feeding tube (model 8888-260406, Sherwood Medical, St. Louis, MO). Insertion depth to the level of the heart was determined by stature (17) with adjustments to obtain the highest temperature reading. Skin temperature was evaluated from seven sites (head, triceps, forearm, chest, thigh, calf, and foot) using copper-constantan thermocouples. Mean weighted T_{sk} was

Table 1: Subject Characteristics, M ± SD

Variable	Male, n = 15	Female, n = 8
Age, yr	22.3 ± 2.9	22.7 ± 3.0
Height, cm	177.8 ± 7.8	166.7 ± 7.5[a]
Weight, kg	78.0 ± 11.8	68.6 ± 13.5
A_D, m^2	1.95 ± 0.17	1.75 ± 0.19[a]
Body fat, %	10.9 ± 2.9	24.1 ± 4.6[a]
$\dot{V}O_{2max}$, ml · kg^{-1} · min^{-1}	46.4 ± 9.2	37.5 ± 13.5

[a] $P < 0.05$, males vs. females.

calculated using the formula of Ramanathan (18). The esophageal and skin temperature thermocouples were interfaced to a datalogger (Omega OM-5000 Data Logger, Omega Engineering, Inc., Stamford, CT) and values were recorded every minute. Expired respiratory air samples were collected and analyzed every min and used to calculate HP [$W \cdot m^{-2}$; Derived from: $[((3.9 \times V_{O_2}) + (1.1 \times V_{CO_2})) \times 60 \times 1.163]/A_D$] (19). Tissue insulation, a derived measure of heat loss, was calculated according to Veicsteinas et al. (20) as insulation ($°C \cdot m^{-2} \cdot W^{-1}$) = $(T_{es} - \overline{T}_{sk}) \times A_D/(0.92\ HP + \Delta T_{es} \times 0.965 \times 0.6 \times wt)$.

Cold water immersion trial. The water immersion protocol consisted of four stages; BASE, pre-occlusion (Pre-OCC), occlusion (OCC), and post-occlusion (Post-OCC). Subjects were dressed only in shorts (males) or shorts and an athletic bra (females).

The CWT entailed the occlusion of extremity blood flow using blood pressure cuffs for 10 min to allow limb blood to cool toward the temperature of the surrounding tissues. Upon release of cuff pressure, the cooled, trapped blood returns to the core region initiating a decrease in T_{es}, with a concomitant increase in HP. The slope of this T_{es}–HP relationship during the dynamic Post-OCC phase is defined as β. In this CWT protocol each subject is immersed to the first thoracic vertebrae with limbs separated and extended on a specially designed chair constructed of PVC tubing. Water temperature of the tank was maintained at 20°C (±0.1°C) via a commercially available chiller (Bath Cooler PBC-2II, NESLAB Instrument Company, Newington, NH). After 40 min, or when T_{es} reached 36.5°C, the OCC stage was initiated. Blood pressure cuffs around the right arm and left leg were inflated to 180 and 220 mmHg, respectively (11,12). After 10 min of blood occlusion, the cuffs were released and the subject remained in the tank for 10 min for (Post-OCC) or until a T_{es} of 35°C. The details of this protocol have been previously described (10).

Statistical analyses: Data were evaluated for differences between menstrual phase, gender, and across time using analysis of variance (ANOVA) procedures. A two-way (phase x time) ANOVA with repeated measures on both factors was used to compare the responses during the menstrual phases. If no differences were detected between menstrual phases, the female data were averaged, and an ANOVA with repeated measures on the time factor was used to analyze gender differences (gender = between, time = within or repeated). Significance was set a priori at $P \leq 0.05$. When significance was observed, a LSD (least significant difference) post-hoc test was used to examine specific contrasts. Changes in T_{es} and HP from 0 to 30, 30–60, and 60–90 min of the CATT were correlated to β obtained during the CWT using Pearson-Product correlations. All values are expressed as means (M) ± standard deviations (SD).

RESULTS

Esophageal temperature: Figure 1 displays the response in T_{es} over time. T_{es} did not demonstrate a main effect for menstrual cycle phase (FOL vs. LUT, $P = 0.838$), thus an ANOVA was performed comparing gender (males vs. females averaging cycle phase as one group). This analysis revealed a significant difference between genders ($P = 0.024$) with females maintaining a higher T_{es}. As expected, a significant main effect for time ($P < 0.001$) was observed. Post-hoc testing revealed that T_{es} was significantly elevated at 5, 15, 30, and 45 min of

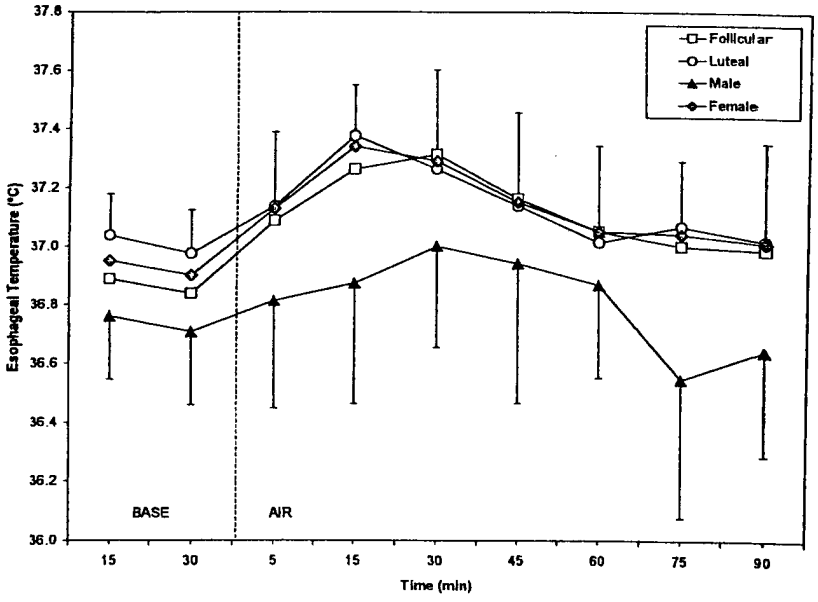

FIG. 1—Response in T_{es} across time (M ± SD).

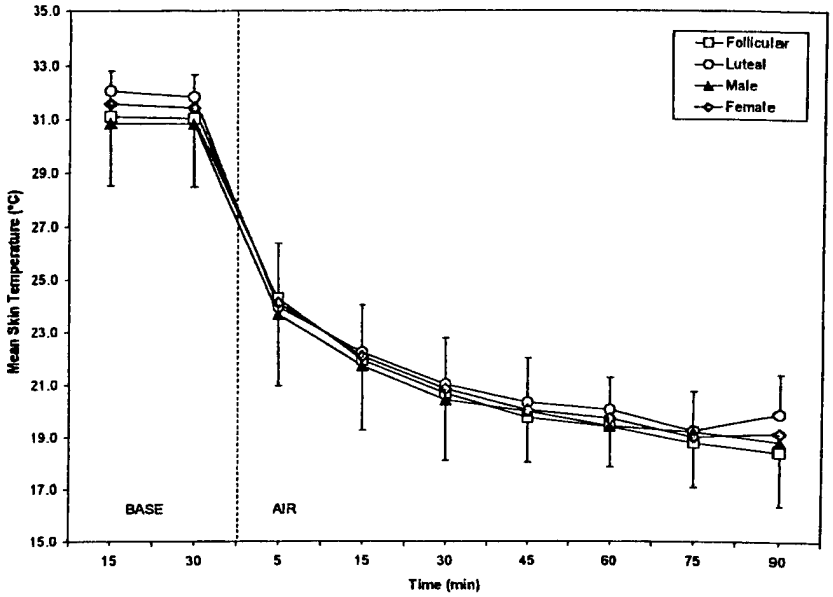

FIG. 2—Response in mean T_{sk} across time (M ± SD).

AIR when compared to BASE values. However, at 60, 75, and 90 min of AIR, T_{es} was not statistically different from BASE values. There was no group x time interaction demonstrated, indicating that the groups changed similarly over time.

Mean skin temperature: Figure 2 displays the response in $\overline{T}_{sk}$ over time. $\overline{T}_{sk}$ did not demonstrate a main effect for menstrual cycle phase (FOL vs. LUT, $P = 0.288$), thus an ANOVA was performed comparing gender (males vs. females averaging cycle phase as one group). This analysis revealed no significant difference between genders ($P = 0.714$). As expected, a significant main effect for time ($P < 0.001$) was observed. Post-hoc testing revealed that $\overline{T}_{sk}$ was significantly different between all time points except for 60 and 75 min and 75 and 90 min. Additionally, $\overline{T}_{sk}$ did not differ between the first and second BASE measurements (i.e., T-15 and T-30, 15 and 30 min of BASE). There was no group × time interaction observed.

Heat production: Figure 3 displays the response in HP over time. HP did not demonstrate a main effect for menstrual cycle phase (FOL vs. LUT, $P = 0.312$), thus an ANOVA was performed comparing gender (males vs. females averaging cycle phase as one group). This analysis did not reveal a significant difference between genders ($P = 0.190$). Again, as expected, a significant main effect for time ($P < 0.001$) was observed. Post-hoc testing revealed that HP was significantly elevated at all time points during AIR compared to BASE. Additionally, HP did not differ between the first and second BASE measurements (i.e., T-15 and T-30, 15 and 30 min of BASE). There was no group x time interaction demonstrated.

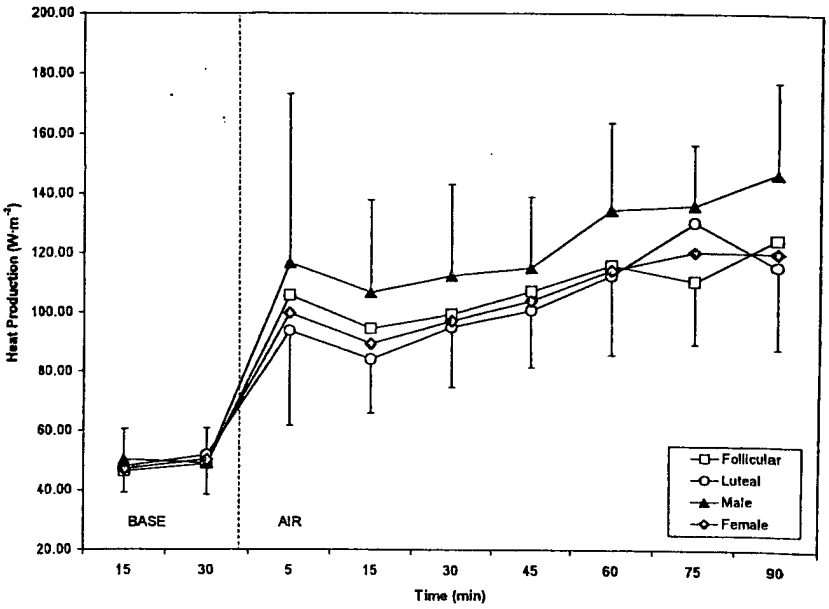

FIG. 3—Response in HP across time (M ± SD).

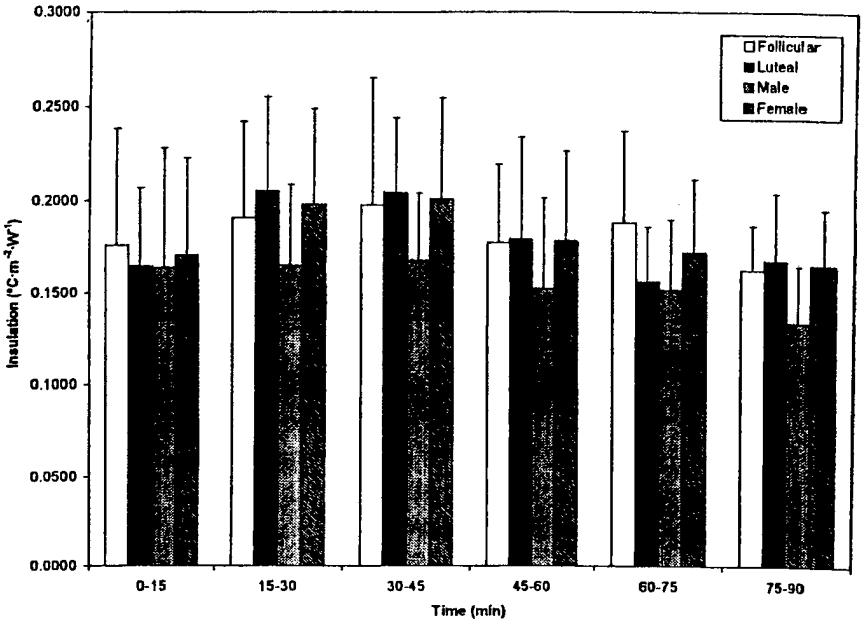

FIG. 4—Insulation for selected time ranges (M ± SD).

Tissue insulation: Figure 4 displays the response in insulation from 0 to15, 15–30, 30–45, 45–60, 60–75, and 75–90 min. Insulation did not demonstrate a main effect for menstrual cycle phase (FOL vs. LUT, $P = 0.776$), thus an ANOVA was performed comparing gender (males vs. females averaging cycle phase as one group). This analysis did not reveal a significant difference between genders ($P = 0.218$; Fig. 4). A significant main effect for time ($P = 0.018$) was observed. Post-hoc testing revealed significant differences between 15–30 and 75–90, 30– 45 and 45–60 and 75–90, and 60–75 and 75–90 min. Additionally, insulation did not differ between the first and second BASE measurements (i.e., T-15 and T-30, 15 and 30 min of BASE). No group x time interaction was demonstrated.

Thermosensitivity and ΔT_{es} and ΔHP: Table 2 displays the correlation coefficients between ΔT_{es} and ΔHP from 0–30, 30–60, and 60–90 min of the CATT and β obtained during a CWT. No significant correlations were observed between β and the changes in T_{es} and HP for the selected time ranges.

DISCUSSION

The purpose of this investigation was to determine whether menstrual cycle phase and gender influence the individual's ability to regulate to the stressor of cold air (5°C for 90 min) and to discern whether β observed during a controlled thermal challenge in 20°C water was related to the responses demonstrated during the CATT. The importance of menstrual cycle phase in assessing the thermoregulation and thermoresponsiveness in females renders investigation.

Rennie and colleagues (21) suggest that the difference in temperature regulation (i.e., the significantly higher T_{es} in females compared to males) may not be due to the disparity in inherent gender differences in overall tissue insulation other than what could be attributed to the inherent differences in subcutaneous fat (1,21). Additionally, Cunningham (8) demonstrated that the thermoregulatory system of females operates at a higher core temperature than males. This observation is in agreement with the core temperature data in the present investigation, whereby women started the experimental trials at a high T_{es} and maintained a higher T_{es} throughout the experimental trial. In contrast to other studies (1,3,4), the present investigation did not find differences in T_{es} over time between the FOL vs. LUT phases. It is possible that the lack of core temperature differences between FOL and LUT demonstrated in females was masked by the stressor imposed by exposure to the cold.

Since there was a significant difference in T_{es} between males and females in the present study, it would be reasonable to assume that the capacity to maintain T_{es} is primarily a function of the different insulative responses between males and females. The calculated insulation values in the present investigation do not demonstrate a gender difference, although it is apparent that the groups did differ in overall percent body fat (i.e., men = 10% body fat vs. women = 25% body fat) and thereby overall tissue insulation. This lack of significant difference in the calculated value for tissue insulation (despite an obvious difference in percent body fat), may be due to the indirect measure of tissue insulation utilized in the present investigation, which is not a direct measurement of heat loss via heat flow disks but rather a derived measure and indirect

Table 2: Correlatioon coefficients and Level of Sugnificance for the Relationship Between β and ΔT_{es} and ΔHP

	ΔT_{es}			ΔHP		
Variable/Time	0–30	30–60	60–90	0–30	30–60	60–90
β, $W \cdot kg^{-1} \cdot °C^{-1}$	−0.260 $P = 0.173$	0.086 $P = 0.658$	0.328 $P = 0.102$	0.1998 $P = 0.303$	0.019 $P = 0.925$	0.167 $P = 0.446$

estimate of actual insulation. The lack of difference in insulation between males and females may lead one to question the estimate of insulation as being a valid measurement.

During acute cold exposure to hypothermic conditions, heat is transferred down the thermal gradient from core to skin across active and passive resistance (22). The active component or vasomotor response may play more of a role for the leaner male individuals, whereas the passive resistance insulative layer offered by subcutaneous adipose tissue (23) may play more of a role in the higher- percent-fat female subjects. While both of these components contribute to the individual's ability to regulate to the stressor of cold, the magnitude that the active and the passive resistances play may differ between males and females in their relative contribution to the maintenance of core temperature. Clearly, since the insulative layer offered by the females in the present study differed from their male counterparts, the passive resistance in this study may have aided the females in the maintenance of a higher T_{es} throughout the cold trial. Therefore, the lack of difference in HP depite differences in T_{es} may be explained by the greater vasomotor response or active resistance in the males and a greater passive resistance in the females, both of which contribute to the thermal gradient and the ability to maintain T_{es}.

From the present data, it appears that β evaluated during cold water immersion does not relate to the change in selected thermal and metabolic parameters during a cold air challenge. This lack of difference may be related to differences in the thermal stressor (cold air vs. cold water) and thereby differing magnitudes of thermal strain and responsiveness (i.e., heat loss via thermal conductivity), morphologic differences between the subjects (during the CATT), as well as variability in the experimental data.

The measure of β (11,12) did not differ between gender or menstrual cycle phase. This lack of significant difference may be explained by the large variability in the data, indicating a large amount of inter-individual variation in β. Therefore, it is difficult to attempt relationships between these data.

Additionally, a limitation of the present investigation is the small sample size and, therefore, the reduced statistical power inherent in this study. However, the majority of the environmental/hypothermia literature does involve very small sample sizes; therefore, the statistical power of those investigations must be considered as well as the difficulty in obtaining subjects to volunteer to participate in this area of research. However, despite the low statistical power of this investigation, statistical significance was found for several dependent variables.

The role of surface area-to-mass ratio in human temperature regulation suggests that in cold conditions, the greater the total body mass, the greater the thermoregulatory benefit due to enhanced tissue insulation and HP. However, since heat transfer occurs from the body surface, a larger surface area promotes greater heat loss (5). Thus, the combination of a large body mass with a small surface area may result in reduction in net heat loss during exposure to hypothermic conditions. Since males and females in the present investigation did not differ in the surface area-to-mass ratio, despite differences in body surface area, the lack of a differential response in HP during resting cold air exposure may be expected. In contrast to resting cold exposure, morphology (i.e., surface area-to-mass ratio, tissue insulation) does not influence β (24). Therefore, the lack of a significant relationship between β (which is not affected by morphologic characteristics) and ΔT_{es} and ΔHP (which may be affected by morphologic characteristics) may not be surprising.

The thermal conductivity of water is approximately 25 times that of still air (7,25). Therefore an individual immersed in cold water will lose heat more than an individual exposed to still air of the same temperature. Even though the air condition and water condition in this experiment differed, the thermal challenge posed by water and air may be due to the different thermal properties posed (and thereby the difference in the rate of change for the thermal variables). For example, an individual immersed in cold water loses heat primarily as a result of conductive heat loss, whereas an individual exposed to cold air loses heat via convection (air movement) as well as conduction. In addition, during cold air exposure there

are less uniform T_{sk} changes due to variations in air movement, posture, and radiant heat loss. Therefore, the poor relationship between the change in the thermal and metabolic variables during the CATT and β may be explained by a combination of factors related to gender differences in T_{es}, or the differing contributions of the passive and active contributions in maintaining temperature homeostasis, or even due to the thermal challenge (air vs. water mediums).

In conclusion, menstrual cycle phase did not cause a differential response in T_{es}, T_{sk}, and HP during a CATT. However, females started and maintained a higher T_{es} than males during the CATT despite similarities in HP and T_{sk}

Also, we found no relationship between β and thermoregulation during the CATT in these subjects.

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Appendix C.

Glickman-Weiss EL, CC Cheatham, N Caine, M Blegen, J Marcinkiewics (In press). The influence of ethnicity on thermosensitivity during cold water immersion. Aviation Space and Environmental Medicine.
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Number of Tables: 2
Number of Figures: 4

THE INFLUENCE OF ETHNICITY ON THERMOSENSITIVITY DURING COLD WATER IMMERSION

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Running Head: Ethnicity and thermosensitivity.

ABSTRACT

Purpose: This investigation evaluated the influence of ethnicity, Caucasian (CAU) vs. African American (AA), on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C) in 15 CAU (22.7 ± 2.7 yr.) vs. 7 AA (21.7 ± 2.7 yr.) males. **Methods:** Following a 20 min baseline period (BASE), subjects were immersed in 20°C water until esophageal temperature (Tes) reached 36.5°C or for a maximum pre-occlusion (Pre-OCC) time of 40 min. Arm and thigh cuffs were then inflated to 180 and 220 mmHg, respectively, for 10 min (OCC). Following release of the inflated cuffs (Post-OCC), the slope of the relationship between the decrease in Tes and the increase in HP was used to define thermosensitivity (ß). **Results:** ANOVA revealed no significant difference in thermosensitivity between CAU and AA (CAU = 3.5± 1.6 vs. AA= 2.4 ± 1.4 $W \cdot kg^{-1} \cdot °C^{-1}$). No significant differences ($p>0.05$) were found for $\overline{T}sk$ (CAU = 24.3± 0.3 vs. AA = 25.1± 0.4°C) or HP ($p>0.05$; CAU = 2.5 ± 0.2 vs. AA = 2.2± 0.3 $W \cdot kg^{-1}$). However, a significant ($p<0.05$) main effect for ethnicity for Tes was observed (CAU = 36.7± 0.1 vs. AA = 36.5± 0.1°C). **Conclusion:** These data suggest, despite a differential response in Tes between AA and CAU groups, the ß of HP during cold water immersion is similar between CAU and AA. Therefore, these data demonstrate that when faced with a cold challenge, there is a similar response in HP between CAU and AA that is accompanied by a differential response in Tes.

Key words: Cold exposure, ethnicity, core temperature, thermoregulation

INTRODUCTION

It is well established that a combination of factors such as gender, body composition, morphology, age, and ethnicity may influence an individual's response to cold stress (10,11, 19, 24). With respect to ethnicity, the focus of this investigation, Scholander et al. (23) observed a greater peripheral cooling without metabolic compensation in Australian Aborigine people while sleeping naked in a cold environment as compared to cold acclimated European males exposed to comparable conditions. In addition, the early work of Rennie and Adams (21) demonstrated that during a cold test (-12°C air with hand and feet bare) the fingers of African Americans (AA) cooled significantly more than those of Caucasian (CAU) subjects, and the increase in metabolism was significantly less in the African American group during acute cold exposure.

However, because of the possible differences in thermal drives (core and skin temperature inputs) between the ethnic groups (i.e., AA vs. CAU), comparisons of thermosensitivity or thermoresponsiveness [i.e., an increase in metabolic heat production (HP) with the controlled manipulation of esophageal temperature (Tes)] has not been adequately determined in differing ethnic groups. One of the difficulties in assessing thermosensitivity of metabolic HP in man is the inability to control for differences in absolute temperatures of both the skin and core thermosensors as well as their rates of cooling, all of which are factors that contribute to the thermogenic response (17). However, the methodology employed in the present investigation will control the experimental conditions (9, 17,18) and selectively manipulate Tes at a constant skin temperature in the quantification of central thermosensitivity (β).

Mittleman and Mekjavic (17,18), validated a technique for evaluating β during cold water immersion. This technique, which controls absolute and dynamic skin temperature by immersion in water, enables core temperature to be manipulated so that the thermoresponsiveness of all subjects are evaluated at similar absolute and dynamic core temperatures. The authors (17,18) evaluated β in European American males (age 23 ± 4 yr) and revealed that the HP response to a similar skin and core thermal drive was unrelated to body composition, size (16), or aerobic fitness (15). Also, recent work from our laboratory has demonstrated that β is similar in CAU males and CAU females 18-30 yr and is not influenced by menstrual cycle phase (i.e. luteal vs. follicular) (9). However, the comparison of β in two of the predominant ethnic groups in the United States population (i.e., AA vs. CAU) has not been studied under controlled experimental conditions. Therefore, comparative data between individuals of non-White origin are limited and renders investigation.

Although the differences in thermal drives and thermal responses have not been explored between AA and CAU individuals, the research literature demonstrates that there are differences in metabolic rate between these groups. Resting metabolic rate, the largest component of total daily energy expenditure, is lower in AA than CAU individuals and also may contribute to a positive energy balance in AA individuals (4, 5, 7).

Since resting metabolic response and energy expenditure have been shown to differ between AA and CAU individuals, differences in the sympathetic-adrenal-medullary (SAM) axis, or the hypothalamic-pituitary axis (HPA) (which produces key hormones that affect fuel utilization and metabolism) could contribute to differences in

thermoresponsiveness (2). Further, there are several physiological factors that influence metabolic rate that are related to the sympathetic nervous system activity (25). These factors include body temperature (22), skeletal muscle metabolism (29), [i.e., plasma concentrations of triiodothyronine (25)], free fatty acids, insulin, and endogenous glucose production (28). Therefore, the central nervous system (CNS), which influences thermoregulation as well as metabolism (via the hypothalamus) has been shown to differ in responsiveness between AA and CAU individuals (28).

In addition to possible differences in thermal responsiveness and resting metabolic rate, research has also demonstrated that AA and CAU individuals differ with respect to body composition (i.e., skeletal muscle characteristics, morphology). Additionally, the peripheral architecture, that is, the skeletal appendicular dimensions and potentially the individual's body composition has been shown to differ between AA and CAU individuals (28). From a thermoregulatory standpoint, the larger an individual's surface area the greater the heat loss to the environment, and thereby the greater the thermal strain for a given environmental condition (11). The difference in lean tissue vs. percent body fat may also contribute to differences in thermoregulation. Fat is a passive resistor to heat exchange, an insulator, and lean tissue is an active tissue that contributes to shivering thermogenesis (and typically higher resting metabolic rates). Thus, these variations in fat and fat-free mass distribution may contribute to differences in thermoregulation and metabolism.

From a military standpoint, there is an urgency to examine non-white individuals since minority groups now comprise approximately 41% of the enlisted army (27). Additionally, the established guidelines for survival in extreme cold environments is

based on research conducted prior to 1980 (27). These survival data focus on the responses of CAU males, 18-30 yr of age, since CAU had previously and primarily comprised the majority of the active duty personnel. However, the demographics of age, gender and ethnicity in the military have undergone a dramatic shift in the past 20 years. Consequently, since the guidelines for cold exposure that presently exist may only represent approximately half of the military personnel and since cold exposure may pose an extreme stress which may result in lethal consequences (7, 24), it is critical to evaluate if differences exist between ethnicities. There is a need to expand our present database on performance in cold environments to those individuals of different ethnicities.

Whether the systematic control of central and peripheral inputs would result in similar core thermosensitivities in AA vs. CAU individuals has not been examined and renders investigation. Therefore, the purpose of the present investigation was designed to evaluate the influence of ethnicity on β of metabolic HP during acute cold exposure.

METHODS

Subjects. Healthy, active CAU men (n=15) and AA men (n=7) age 18-29 yr, volunteered to participate in the study (Table 1) and provided informed consent. The Institutional Review Board approved all experimental procedures for Human Subjects Research. Subjects completed the cold trials between April and mid-November to limit the potential influence of natural cold acclimatization on physiological responses (3).

Insert Table 1

Pre-experimental Testing. During the first visit to the laboratory, anthropometric variables and maximal oxygen uptake ($\dot{V}O_{2max}$) were measured. Height and weight were measured via a stadiometer and a balance beam scale, respectively. Skinfold thickness was measured using standardized procedures and percent body fat was calculated using a gender specific equation (13). Surface area (A_D) was calculated from height and weight using the formula of DuBois and DuBois (6).

Each subject performed a maximal exercise test on a magnetically braked cycle ergometer to determine $\dot{V}O_{2max}$. The protocol consisted of increasing the work rate in a progressive manner until maximal voluntary exhaustion was achieved. The test began at 60 W for 2 min and increased 20 $W \cdot min^{-1}$ thereafter. Oxygen consumption ($\dot{V}O_2$) was measured using an automated open circuit system (MAX-1 CART, Physio-Dyne Instrument Company, Quogue, NY). Expired respiratory air samples were collected continuously throughout the maximal exercise test and recorded at 30-sec intervals. Heart rate (HR) was recorded every 30 sec via telemetry (Vantage XL, Polar Electro Inc., Woodbury, NY) and rating of perceived exertion (RPE) was assessed during the last 10 sec of each exercise stage. $\dot{V}O_{2max}$ was determined to be the average of the two greatest 30 sec values.

Water Immersion Protocol. The water immersion protocol consisted of 4 stages; baseline (BASE), pre-occlusion (Pre-OCC), occlusion (OCC), and post-occlusion (Post-OCC). Subjects were dressed only in shorts.

Throughout the water immersion protocol, esophageal temperature (Tes), skin temperature, expired respiratory air samples, and HR were continuously measured. Tes was measured using a copper-constantan thermocouple encased in an infant feeding tube (Model # 8888-260406, Sherwood Medical, St. Louis, MO). Insertion depth to the level of the heart was determined by sitting stature (14) with adjustments to obtain the highest temperature reading. Skin temperature was evaluated from 7 sites (head, tricep, hand, chest, thigh, calf, foot) using copper-constantan thermocouples. Mean weighted skin temperature ($\bar{T}sk$) was calculated using the formula of Hardy and DuBois (12). The esophageal and skin temperature thermocouples were interfaced to a datalogger (Omega OM-5000 Data Logger, Omega Engineering, Inc., Stamford, CT) and values were recorded every minute. Expired respiratory air samples were collected and analyzed every minute and used to calculate HP ($W \cdot m^{-2}$ or $W \cdot kg^{-1}$). HR was recorded every minute.

During BASE, each subject sat quietly in a semi-recumbent position on a lounge chair for 20 min in 28°C air. Following BASE, each subject was escorted to the immersion tank to begin the Pre-OCC stage of the water immersion protocol. Each subject sat immersed to the first thoracic vertebrae with limbs separated and extended on a specially designed chair constructed of PVC tubing. Water temperature of the tank was maintained at 20°C (± 0.1°C) via a commercially available chiller (Bath Cooler PBC-2II, NESLAB Instrument Company, Newington, NH). After 40 min, or when Tes reached 36.5°C, the OCC stage was initiated. Blood pressure cuffs around the right arm and left leg were inflated to 180 and 220 mmHg, respectively (17,18). After 10 min of blood occlusion, the cuffs were released and the subject remained in the tank for 10 min (Post-

OCC) or until a Tes of 35°C. Upon release of the cuffs, Tes decreased resulting from the return of the cooled extremity blood to the core region, while HP concomitantly increased. The slope of the stimulus (decrease in Tes) – response (increase in HP) relationship during the Post-OCC phase was used to define β ($W \cdot kg^{-1} \cdot °C^{-1}$). Following the Post-OCC stage, subjects were removed from the immersion tank and escorted to a warm shower for rewarming.

Statistical Analyses. Data were evaluated for differences between groups (CAU vs. AA) and across time using a two-way (2 x 4) analysis of variance (ANOVA) with repeated measures on the time factor. Significance was set *a priori* at $p < 0.05$. When significance was observed, a Tukey post-hoc test was used to examine specific contrasts. *A priori* contrasts on the physiological responses at baseline were compared using a Tukey post-hoc test. All values are expressed as means (M) ± standard deviations (SD). HP (determined via $\dot{V}O_2$ and corrected for R) was analyzed and is expressed as $W \cdot kg^{-1}$ and $W \cdot m^{-2}$ and ß was analyzed and is reported as both $W \cdot kg^{-1} \cdot °C^{-1}$ and $W \cdot m^{-2} \cdot °C^{-1}$. Both units of measurement are presented so as to make comparisons with the available experimental literature. Lastly, due to the unequal group sizes, Levene's Test for Equality of Variances was used to determine whether group variances were unequal. If the groups exhibited different variances, an adjusted p-value was used.

RESULTS

Physiological Responses During Baseline

There were no significant differences observed in Tes between the CAU and AA (36.9±0.2 vs. 36.8± 0.2°C, respectively). HP was not significantly different between the CAU and AA males when HP was expressed relative to body weight (1.3± 0.2 vs. 1.3± 0.3 $W \cdot kg^{-1}$, respectively) or A_D (53.4 ± 8.1 vs. 54.7± 13.0 $W \cdot m^{-2}$, respectively). $\bar{T}sk$ also did not differ between CAU vs. AA (31.7±0.8 vs. 31.7±0.9°C, respectively) during baseline.

Physiological Responses During Cold Water Immersions

Heat production (HP). HP did not demonstrate a main effect for ethnicity ($p = 0.285$) when expressing HP in terms of $W \cdot kg^{-1}$ (CAU= 2.5 ± 0.8 vs. AA= 2.2 ± 0.8 $W \cdot kg^{-1}$), or when expressing HP in $W \cdot m^{-2}$ (Table 2: $p = 0.37$). A significant main effect for time ($p < 0.001$) was observed when HP was expressed in either $W \cdot kg^{-1}$ or $W \cdot m^{-2}$ whereby HP exhibited a characteristic elevation during the onset of immersion followed by a slight decrease or plateau during the Pre-OCC and OCC stages and then an increase during the Post-OCC stage (Figure 1). Post-hoc analysis revealed significant differences between all time periods except for Pre-OCC and OCC (Table 2). Additionally, there was no

significant group x time interaction demonstrated.

Insert Table 2, Figure 1

Esophageal temperature (Tes). Tes demonstrated a main effect for ethnicity ($p = 0.003$) (CAU = 36.7± 0.2 vs. AA = 36.4± 0.2°C). Also, as expected a significant main effect for time was observed ($p < 0.001$) (Figure 2, Table 2). Post-hoc testing revealed significant differences between Pre-OCC and OCC, Pre-OCC and Post-OCC, and, OCC and Post-OCC only (Table 2). Additionally, there was no significant group x time interaction demonstrated.

Insert Figure 2

Mean skin temperature ($\bar{T}sk$). $\bar{T}sk$ demonstrated a trend for the main effect of ethnicity ($p = 0.089$) (CAU = 24.2 ± 1.1 vs. AA = 25.1 ± 0.1.1C). Figure 3 displays the response in $\bar{T}sk$ over time. As expected, a significant main effect for time ($p < 0.001$) was observed and subsequent post-hoc testing revealed differences between all time points except for OCC and Post-OCC. (Table 3). Additionally, there was no significant group x time interaction demonstrated.

Insert Figure 3

Central Thermosensitivity (ß). The relationship between the decrease in Tes and increase in HP following the release of occlusion and subsequent recirculation of the cooled extremity blood is depicted in Figure 4. All values for ß are given as absolutes. ß was higher in the CAU group than the AA group but this difference did not reach statistical significance ($p = 0.14$). When expressed relative to A_D (for experimental comparisons), ß was again not significant between the CAU vs. AA groups ($p= 0.51$; 121.8 ±63.4 vs. 100.8 ± 65.6, respectively).

Insert Figure 4

DISCUSSION

In the present study, thermal and metabolic responses were evaluated during immersion in 20°C water following the alteration in blood circulation (by pressure cuff occlusion). The experimental manipulation of Tes by pressure cuff occlusion and the subsequent release of the cooled trapped extremity blood, resulted in an increase in shivering thermogenesis and a reduction in Tes. These observations have been reported previously (17,18). The slope of the Tes-HP relationship during the dynamic Post-OCC phase that defines β did not significantly differ between CAU and AA. This study extends the work of Mittleman and Mekjavic (17,18) by employing a sample of males of different ethnicities. Values for β in the present investigation were similar to those previously reported by Mittleman et al. (17,18) (males: 4.45 ± 0.55 $W \cdot kg^{-1} \cdot °C^{-1}$; CAU = 3.56 ± 1.62 $W \cdot kg^{-1} \cdot °C^{-1}$; AA = 2.43 ± 1.63 $W \cdot kg^{-1} \cdot °C^{-1}$). The lack of significant

difference may be explained by the large variability in the data, indicating that there is a large amount of inter-individual variation in β. The variability in β was similar to that observed in previous studies (17,18).

Although the present investigation did find a difference between Tes in CAU and AA, this differential response was unaccompanied by differences in $\bar{T}sk$, HP ($W \cdot m^{-2}$ or $W \cdot kg^{-1}$) and ß. Although not significantly different, HP ($W \cdot kg^{-1}$) was higher in CAU compared to AA, a finding that is consistent with the experimental literature (5, 7, 28). However, HP did not differ during BASE between CAU and AA. Chitwood et al. and others (7, 28) have demonstrated that AA individuals demonstrate a lower resting energy expenditure as well as an attentuated energy expenditure during exercise and recovery from an exercise bout compared to CAU individuals. The lack of significant difference in this investigation may be due to the measure of "baseline data" not actually reflecting true resting energy expenditure (REE). The anticipation of the water immersion protocol may have caused a higher rate of energy expenditure (anticipatory effect) and may have masked a differential response.

Centrally, external ambient stressors influence homeostasis by altering the involvement of the hypothalamus with both the SAM and the HPA axes (2). The distinct effects of these two hormonal axes compliment each other (2), and the primary hormone products of these axes are epinephrine, norepinephrine, and cortisol. These hormones serve to mobilize and distribute metabolic fuels at different rates. This in part may explain the results of others (5, 7, 28) that have shown that fuel utilization and metabolism differ between CAU and AA individuals. Thus, the lower Tes and HP (trend) demonstrated in the AA group in this investigation may be centrally mediated.

The hypothalamus is the site of control for many biological responses including temperature, thirst, and hunger. This site, in concert with the suprachiasmatic nucleus (SCN: which regulates many neuroendocrine rhythms including ACTH, thyroid stimulating hormone, insulin and glucagon), may influence the individual's biological rhythms (26). Since the utilization of insulin and glucagon have been shown to differ between AA vs. CAU individuals (5, 7, 28), there may be a disparity in the influence of the hypothalamus (temperature regulation) and the SCN on maintaining temperature homeostasis in AA vs. CAU individuals. Therefore, subsequent work may include the exploration of the aforementioned blood markers to more closely examine thermoregulatory mechanisms and disparities.

The lack of difference in $\overline{T}sk$ may indicate that despite differences in Tes, $\overline{T}sk$ was maintained similarly by both CAU and AA perhaps indicating a similar degree of peripheral vasoconstriction. This finding is in contrast to the earlier work of Adams and Covino (1) who reported lower average skin temperatures reached by AA prior to the onset of shivering and the subsequent increase in HP. However, in the present investigation the cold stressor was water. During cold water immersion, skin temperature typically mimics water temperature. The previous work of Rennie and Adams (21) was conducted in air which is a less uniform cold stressor due to variations in air movement, posture and radiant heat loss.

Body temperature depends on the dynamic balance between heat gained through metabolic HP and heat lost to the environment. When heat loss exceeds heat gain there is a decline in core temperature. Since the AA group exhibited a lower overall Tes than their CAU counterparts, it is likely that the lack of a significant differential response in

HP created a greater thermal strain and contributed to the lower Tes. This observation is in agreement with the early work of Rennie and Adams (21) and Adams and Covino (1) who demonstrated a lower rise in metabolic rate during cold exposure in AA compared to CAU individuals. Furthermore, Rennie and Adams (21) reported an increase in shivering later (during exposure), or at a reduced core temperature in AA compared to than their CAU counterparts. Therefore, shivering thermogenesis (as reflected by HP) was lower in the AA group, and may have contributed to the lower Tes exhibited.

Adams and Covino (1) reports that the failure of his AA group to increase HP as soon as or as quantitatively as high as CAU or Eskimos when exposed to cold (air temperature of 17°C for 85 min) is indicative of an increased susceptibility to cold injury. Though Tes differed between groups in the present investigation, the lack of significant difference between thermoresponsiveness or β between the CAU and AA groups, whereby, Tes and HP are both manipulated systematically may suggest otherwise.

The determination of β allows for the assessment of group differences (CAU vs. AA) in the physiological responses to a decrease in core temperature regardless of the anthropometrical or morphological differences (8, 20). Therefore, the determination of β may reveal whether or not certain individuals or groups of individuals are at a marked disadvantage during cold exposure. If a marked disadvantage was observed, this information could lead to alterations in acceptable exposure time, equipment / insulation needs, or in the guidelines set forth to protect the individual from cold related injuries.

In conclusion, these data suggest that the β of HP during cold water immersion is similar between AA and CAU, although a lower Tes was observed throughout the cold water trial in the AA.

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FIGURE LEGENDS

Figure 1: Mean values for heat production (M±SD): During baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow in Caucasian (CAU) vs. African American (AA), ($p = 0.108$).

Figure 2: Mean values for esophageal temperature (M±SD): During baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow in Caucasian (CAU) vs. African American (AA), ($p = 0.079$).

Figure 3: Mean values for skin temperature (M±SD): During baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow in Caucasian (CAU) vs. African American (AA), ($p = 0.068$).

Figure 4: Comparison of values for thermosensitivity (M±SD) between Caucasian (CAU) and African American (AA), ($p = 0.51$)

Table 1. Subject characteristics (M ± SD).

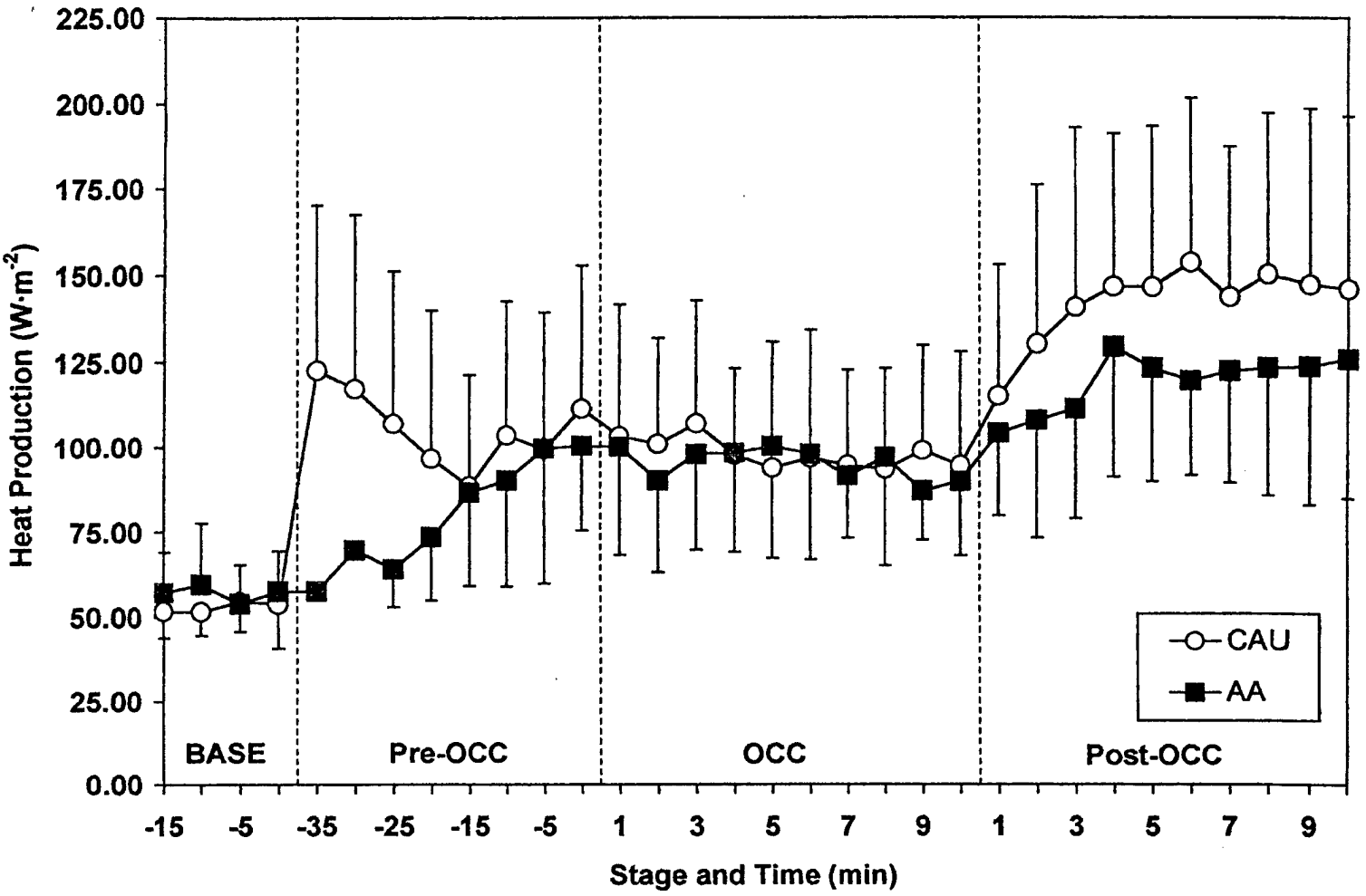
Variable	CAU (n=15)	AA (n=7)
Age (yrs)	22.7 ± 2.8	21.7 ± 2.7
Height (cm)	177.7 ± 7.9	183.1 ± 8.3
Weight (kg)	79.0 ± 11.1	86.8 ± 13.4
BSA (m^2)	1.96 ± 0.16	2.07 ± 0.17
Body fat (%)	10.9 ± 2.9	12.5 ± 5.4
$\dot{V}O_2max$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	46.4 ± 9.2	42.1 ± 8.8

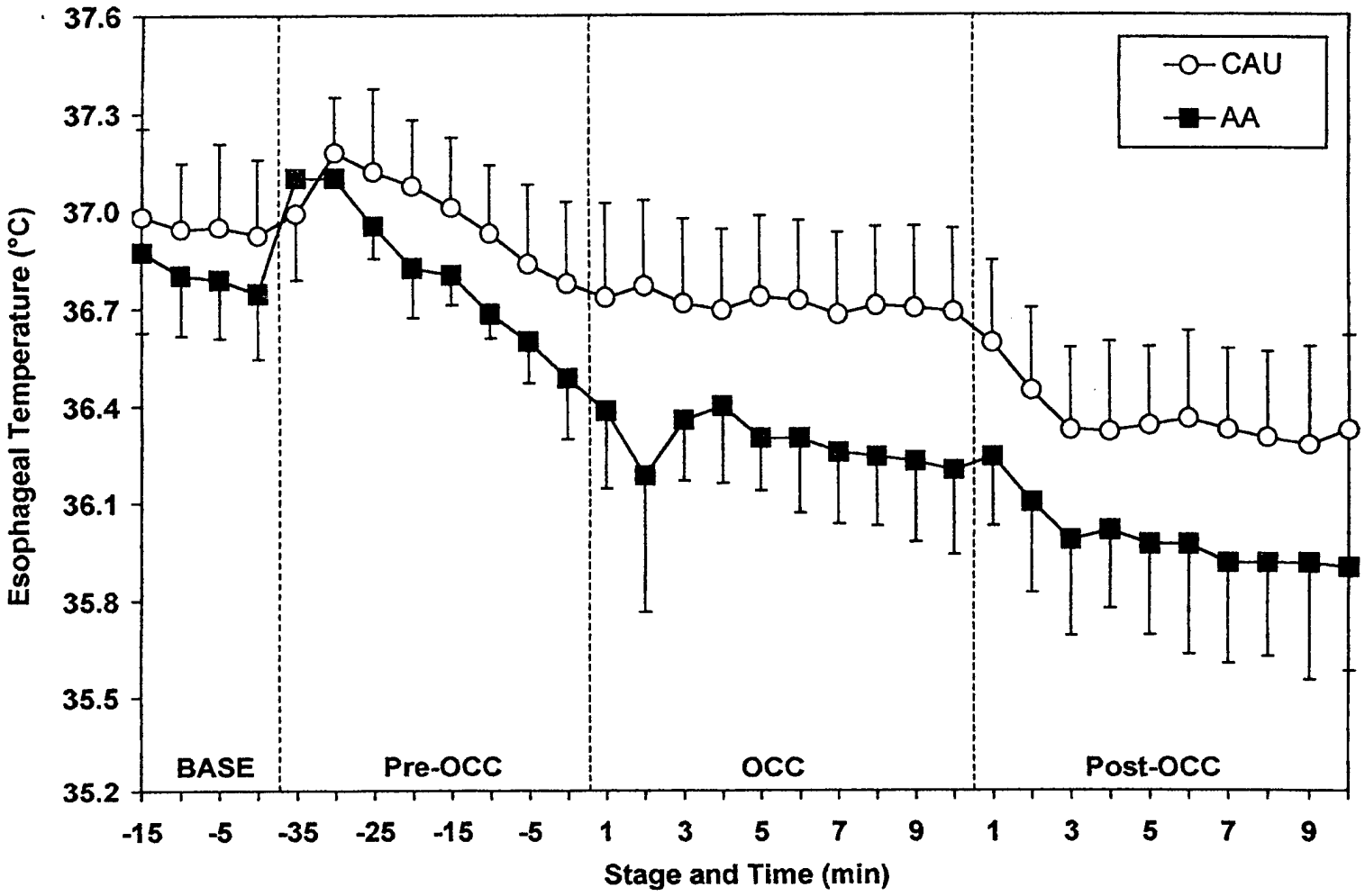
BSA, Body Surface Area; * $p < 0.05$, CAU vs. AA.

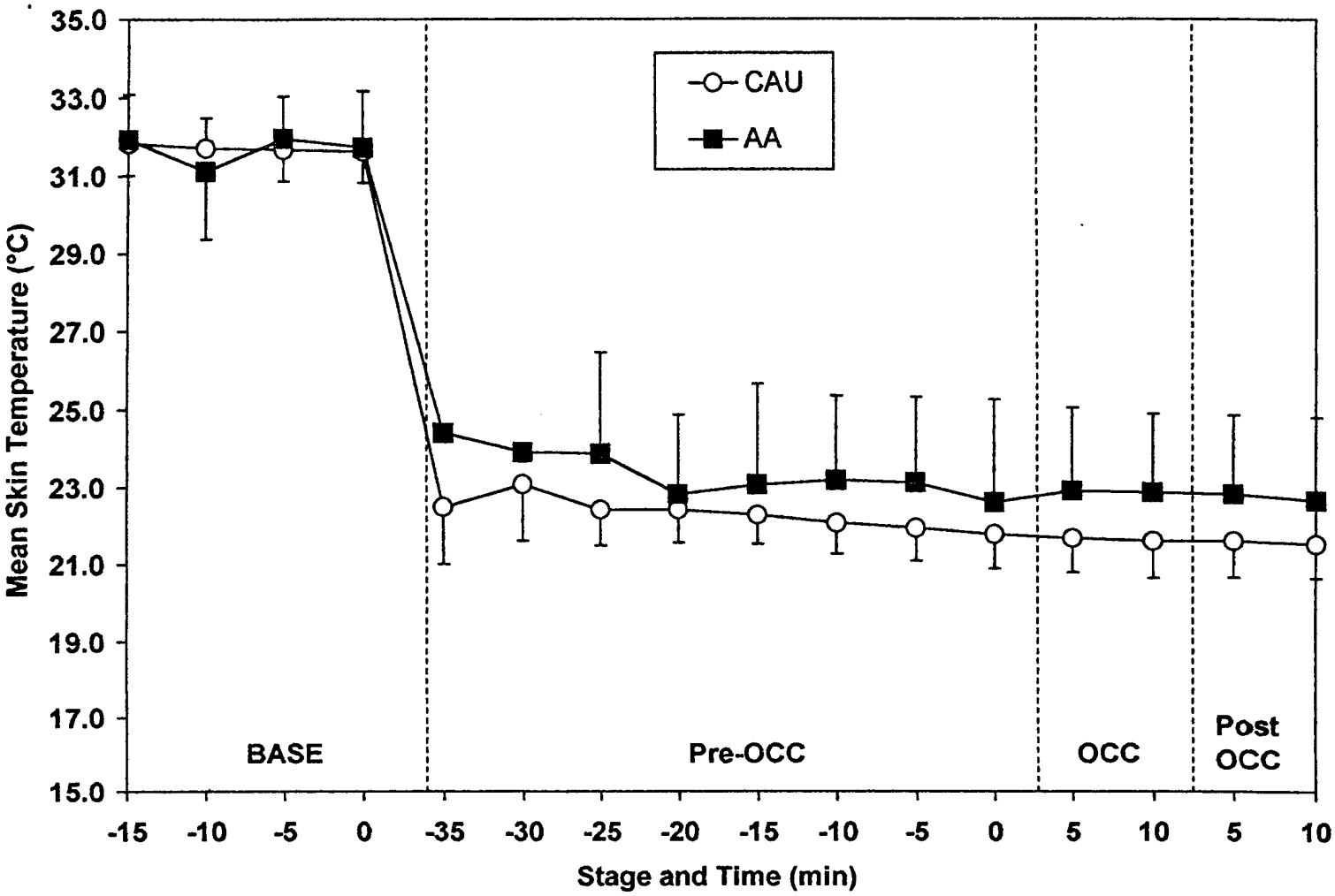
Table 2. Esophageal temperature (Tes), mean skin temperature ($\bar{T}sk$), and heat production (HP) across time (M ± SD).

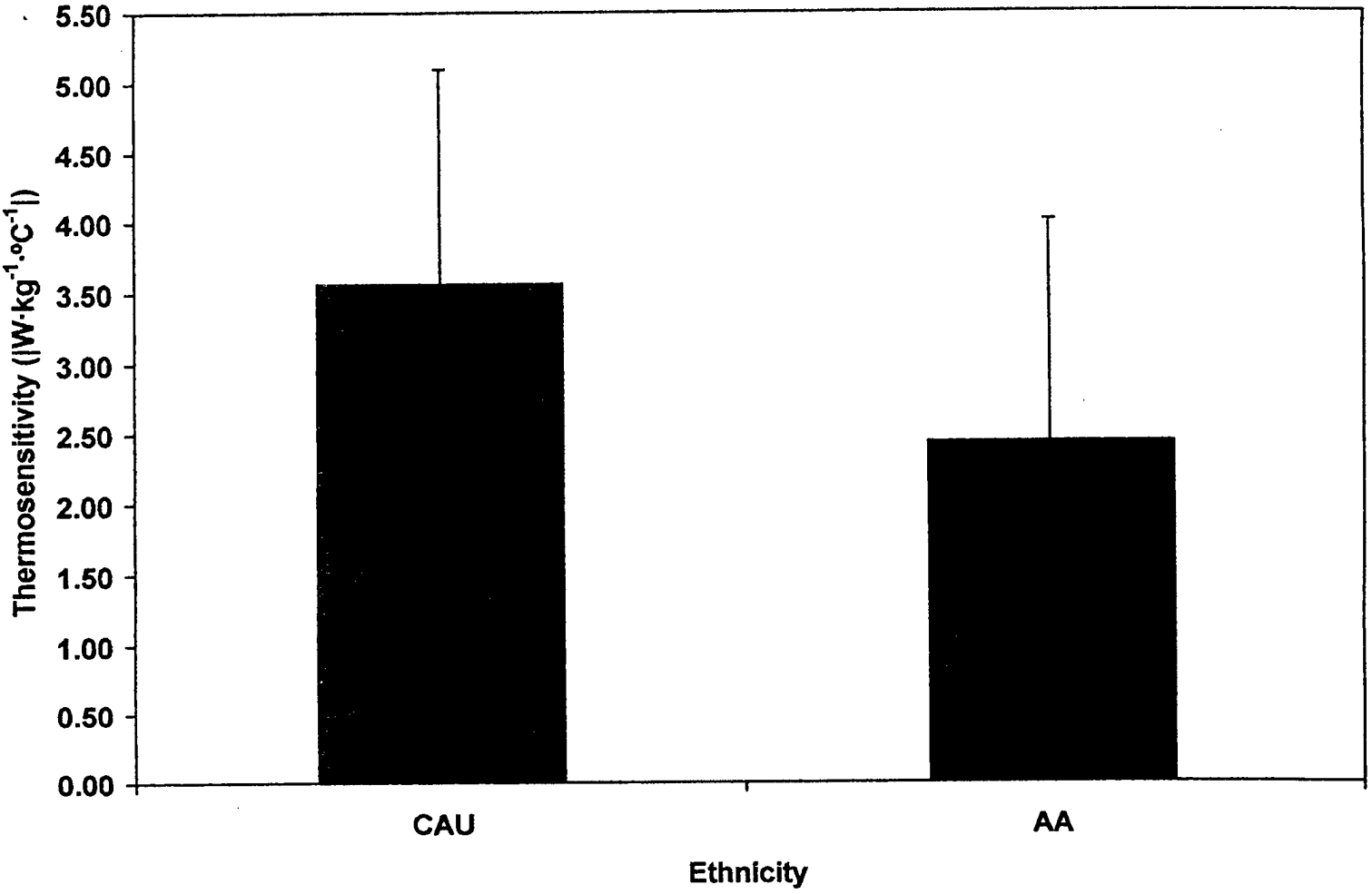
	Tes (°C)			$\bar{T}sk$ (°C)			HP ($W \cdot m^{-2}$)		
Stage	**CAU**	**AA**	**Total**	**CAU**	**AA**	**Total**	**CAU**	**AA**	**Total**
BASE	37.0 ± 0.2	36.8 ± 0.2	36.9 ± 0.2	31.7 ± 0.8	31.7 ± 1.0	31.7^{def} ± 0.9	53.36 ± 8.14	54.71 ± 13.04	53.79^{ijk} ± 9.66
PRE-OCC	36.9 ± 0.2	36.7 ± 0.2	36.8^{*ac} ± 0.2	22.1 ± 0.9	23.2 ± 2.3	22.4^{dgh} ± 1.5	105.13 ± 36.67	91.45 ± 22.58	100.78^{il} ± 32.93
OCC	36.7 ± 0.2	36.3 ± 0.2	36.6^{ab} ± 0.3	21.6 ± 0.9	22.9 ± 2.1	22.0^{eg} ± 1.5	97.92 ± 28.84	94.68 ± 24.08	96.89^{jm} ± 26.88
POST-OCC	36.4 ± 0.3	36.0 ± 0.3	36.2^{bc} ± 0.3	21.5 ± 0.9	22.7 ± 2.1	21.9^{fh} ± 1.5	141.73 ± 42.97	115.21 ± 33.13	133.30^{klm} ± 41.29

CAU, Caucasian; AA, African-American; BASE, Baseline; PRE-OCC, Pre-occlusion; OCC, occlusion; POST-OCC, post-occlusion.
* Means with same superscripts differ ($p < 0.05$).


225.00
200.00
175.00
150.00
125.00
100.00
75.00
50.00
25.00
0.00
Heat Production (W·m-2)
BASE
Pre-OCC
OCC
Post-OCC
-15
-5
-35
-25
-15
-5
1
3
5
7
9
1
3
5
7
9
Stage and Time (min)
CAU
AA


37.6
37.3
37.0
36.7
36.4
36.1
35.8
35.5
35.2
Esophageal Temperature (°C)
CAU
AA
BASE
Pre-OCC
OCC
Post-OCC
-15
-5
-35
-25
-15
-5
1
3
5
7
9
1
3
5
7
9
Stage and Time (min)


35.0
33.0
31.0
29.0
27.0
25.0
23.0
21.0
19.0
17.0
15.0
Mean Skin Temperature (°C)
CAU
AA
BASE
Pre-OCC
OCC
Post OCC
-15
-10
-5
0
-35
-30
-25
-20
-15
-10
-5
0
5
10
5
10
Stage and Time (min)


5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
Thermosensitivity (|W·kg-1·°C-1|)
CAU
AA
Ethnicity

Appendix D.

Glickman EL, N Caine, CC Cheatham, M Blegen. (In review) The influence of age on thermosensitivity during cold water immersion
(pages 57-81)

THE INFLUENCE OF AGE ON THERMOSENSITIVITY DURING COLD WATER IMMERSION

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Running Head: The influence of age on thermosensitivity.

ABSTRACT

This investigation evaluated the influence of age old (OLD) vs. young (YNG), on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C) in 15 YNG (22.7 ± 2.7 yr.) vs. 7 OLD (21.7 ± 2.7 yr.) individuals. Following a 20 min baseline period (BASE), subjects were immersed in 20°C water until esophageal temperature (Tes) reached 36.5°C or for a maximum pre-occlusion (Pre-OCC) time of 40 min. Arm and thigh cuffs were then inflated to 180 and 220 mmHg, respectively, for 10 min (OCC). Following release of the inflated cuffs (Post-OCC), the slope (ß) of the relationship between the decrease in Tes and the increase in HP was used to quantify thermosensitivity. ANOVA revealed no significant difference in thermosensitivity between OLD and YNG (OLD = 2.25± 1.72 vs. YNG= 3.56 ± 1.53 $W \cdot kg^{-1} \cdot °C^{-1}$). No significant differences ($p>0.05$) were found for Tsk (OLD = 23.8± 0.31 vs. YNG = 24.2± 0.19°C), HP ($p>0.05$; OLD = 3.10± 0.38 vs. YNG = 2.50± 0.22 $W \cdot kg^{-1}$) or Tes (OLD = 36.61± 0.11 vs. YNG = 36.74± 0.06°C). Therefore, these data demonstrate that when faced with a cold challenge, there is a similar response in ß, HP, Tes and Tsk between OLD and YNG individuals.

Key words: Cold exposure, ethnicity, core temperature, thermoregulation

INTRODUCTION

It is well established that a combination of factors such as gender, body composition, morphology, age, and ethnicity may influence the individual's ability to respond to the stressor of cold (Glickman-Weiss et al. 1991, Glickman-Weiss et al. 1993, Mittleman 1990, Nunneley 1978). With respect to age, the focus of this investigation, there are numerous age-related changes that occur that may compromise one's ability to thermoregulate during acute cold exposure (Kenney and Buskirk 1995, Keys 1973, Schaefer et al. 1996). These changes include an attenuated core and mean skin temperature response for a given thermal challenge (Fox et al. 1973), a reduced ability to conserve body heat through cutaneous vasoconstriction (Richardson et al. 1992), as well as a reduction in tissue insulation, lean body mass and resting metabolic rate. As a consequence, these age-related changes place the older individual at a greater risk for cold injury.

Frank et al. (2000) examined thermoregulatory differences in younger and older human subjects utilizing a protocol designed to decrease core temperature via intravenously administration of cold fluid (40 ml/kg, 4°C) over 30 min in young (18-23 yr. old) vs. older (55-71 yr. old) individuals. Plasma norepinephrine (NE) increased fourfold in the younger but only twofold in the older subjects. Since cold-induced changes in vasomotor tone depend on NE release, the impairment in thermoregulatory vasoconstriction with aging may be due to the decrease in NE release (or a decrease in vasomotor response for a given amount of NE at its receptors). Frank (2000) demonstrated that the vasomotor response for a given plasma NE concentration was decreased in the older group, compared with the younger group and the older group had

significantly lower core temperature thresholds for vasoconstriction. Since both vasoconstriction and shivering are critical responses that play a role in the maintenance of body temperature during a cold challenge, and these mechanisms may be reduced with aging, (due to vasomotor, metabolic and morphological changes that occur with aging), it follows that temperature regulation may therefore be reduced with aging as well.

Furthermore, the older adult is less capable of subjectively sensing thermal perception (Collins et al. 1981, Fitzgerald and Jessop 1981). For example, the older adult is capable of sensing a 2.5°C change in ambient temperature while the younger adult can discern a difference in ambient temperature of 0.8°C (Collins 1987). Therefore, the older adult when exposed to the cold is less able to sense changes in environmental extremes, as well as responding physiologically to maintain temperature homeostasis as compared to their younger counterparts. This may exacerbate the older individual's chance of not only being exposed to a more stressful (cold) environment but also, creates a higher risk for cold injury, as their ability to respond to a cold challenge is also physiologically reduced.

However, because of the possible differences in thermal drives (core and skin temperature inputs) between the age groups (i.e., young =18-30 yr. vs. old= 40-50 yr. old), comparisons of thermosensitivity or thermoresponsiveness [i.e., an increase in metabolic heat production (HP) with the controlled manipulation of esophageal temperature (Tes)] has not been adequately determined in differing age groups. One of the difficulties in assessing thermosensitivity of metabolic HP in man is the inability to control for differences in absolute temperatures of both the skin and core thermosensors as well as their rates of cooling, all of which are factors that contribute to the thermogenic

response (Mittleman 1990). However, the methodology employed in the present investigation will control the experimental conditions (Mittleman 1990, Mittleman and Mekjavic 1988) and selectively manipulate Tes at a constant skin temperature in the quantification of central thermosensitivity (β).

Mittleman and Mekjavic (1988), validated a technique for evaluating β during cold water immersion. This technique, which controls absolute and dynamic skin temperature by immersion in water, enables core temperature to be manipulated so that the thermoresponsiveness of all subjects are evaluated at similar absolute and dynamic core temperatures. The authors (Mittleman and Mekjavic 1988, 1991) evaluated β in European American males (age 23 ± 4 yr) and revealed that the HP response to a similar skin and core thermal drive was unrelated to body composition, size (Mittleman 1990), or aerobic fitness (Mittleman 1990a). Also, recent work from our laboratory has demonstrated that β is similar in CAU males and CAU females 18-30 yr and is not influenced by menstrual cycle phase (i.e. luteal vs. follicular) (Glickman-Weiss et al. 2000). However, the comparison of β in older vs. younger individuals groups in the United States population has not been studied under controlled experimental conditions. Therefore, comparative data between individuals varying by age are limited and renders investigation.

Although the differences in thermal drives and thermal responses have not been explored between older vs. younger individuals, the research literature demonstrates that there are differences in metabolic rate between these groups. Resting metabolic rate (RMR), the largest component of total daily energy expenditure, is lower in older than younger individuals and also may contribute to a positive energy balance in older

individuals (Visser et al. 1995). RMR is known to decrease with increasing age (Keyes et a. 1973), mainly because of a change in body composition. Fat free mass decreases with age and because this mass is metabolically active, the RMR is likely to decrease (Tzankoff and Norris 1977) as well. Also, a lower physical activity level (total energy expenditure) and hormonal changes might also contribute to a lower RMR in older individuals (Schwartz et al. 1990, Poehlman et al. 1992).

Since resting metabolic response and energy expenditure have been shown to differ between older and younger individuals, differences in the sympathetic-adrenal-medullary (SAM) axis, or the hypothalamic-pituitary axis (HPA) (which produces key hormones that affect fuel utilization and metabolism) could contribute to differences in thermoresponsiveness (Armstrong 2000). Further, there are several physiological factors that influence metabolic rate that are related to the sympathetic nervous system activity (Toubro et al. 1996). These factors include body temperature (Rising 1992), skeletal muscle metabolism (Zurlo 1990), [i.e., plasma concentrations of triiodothyronine (Toubro 1996)], free fatty acids, insulin, and endogenous glucose production (Weyer 1992). Therefore, the central nervous system (CNS), which influences thermoregulation as well as metabolism (via the hypothalamus) has been shown to differ in responsiveness between older vs. younger individuals (Weyer 1992).

From a military standpoint, there is an urgency to examine older individuals since older individuals now comprise approximately 10% of the active duty army personnel (DMDC Data, 1997). Additionally, the established guidelines for survival in extreme cold environments is based on research conducted prior to 1980. These survival data focus on the responses of CAU males, 18-30 years of age, since CAU had previously and

primarily comprised the majority of the active duty personnel. However, the demographics of age, gender and ethnicity in the military have undergone a dramatic shift in the past 20 years. Consequently, since the guidelines for cold exposure that presently exist may only represent approximately half of the military personnel and since cold exposure may pose an extreme stress which may result in lethal consequences (Toner and McArdle 1988), it is critical to evaluate if differences exist between age groups. There is a need to expand our present database on performance in cold environments to those individuals of different ages.

METHODS

Subjects. Healthy, active YNG men (n= 15, 18-30 yr.) and OLD men (n=7, 40-55 yr.) volunteered to participate in the study (Table 1) and provided informed consent. The Institutional Review Board approved all experimental procedures for Human Subjects Research. Subjects completed the cold trials between April and mid-November to limit the potential influence of natural cold acclimatization on physiological responses (Burton 1955).

Insert Table 1

Pre-experimental Testing. During the first visit to the laboratory, anthropometric variables and maximal oxygen uptake (VO_{2max}) were measured. Height and weight were measured via a stadiometer and a balance beam scale, respectively. Skinfold thickness

was measured using standardized procedures and percent body fat was calculated using a gender specific equation (Jackson and Pollock 1978). Surface area (A_D) was calculated from height and weight using the formula of DuBois and DuBois (1915).

Each subject performed a maximal exercise test on a magnetically braked cycle ergometer to determine VO_{2max}. The protocol consisted of increasing the work rate in a progressive manner until maximal voluntary exhaustion was achieved. The test began at 60 W for 2 min and increased 20 W per min thereafter. Oxygen consumption (VO_2) was measured using an automated open circuit system (MAX-1 CART, Physio-Dyne Instrument Company, Quogue, NY). Expired respiratory air samples were collected continuously throughout the maximal exercise test and recorded at 30-sec intervals. Heart rate (HR) was recorded every 30 sec and rating of perceived exertion (RPE) was assessed during the last 10 sec of each exercise stage. VO_{2max} was determined to be the average of the two greatest 30-sec values.

Water Immersion Protocol. The water immersion protocol consisted of 4 stages; baseline (BASE), pre-occlusion (Pre-OCC), occlusion (OCC), and post-occlusion (Post-OCC). Subjects were dressed only in shorts.

Throughout the entire water immersion protocol, core (esophageal) temperature (Tes), skin temperature, expired respiratory air samples, and HR were continuously measured. Tes was measured using a copper-constantin thermocouple encased in an infant feeding tube (Model # 8888-260406, Sherwood Medical, St. Louis, MO). Insertion depth to the level of the heart was determined by sitting stature (Mekjavic and Rempel 1990) with adjustments to obtain the highest temperature reading. Skin

temperature was evaluated from 7 sites (head, tricep, forearm, hand, chest, thigh, calf, foot) using copper-constantine thermocouples. Mean weighted skin temperature (Tsk) was calculated using the formula of Hardy and DuBois (1938). The esophageal and skin temperature thermocouples were interfaced to a datalogger (Omega OM-5000 Data Logger, Omega Engineering, Inc., Stamford, CT) and values were recorded every minute. Expired respiratory air samples were collected and analyzed every minute and used to calculate HP ($W \cdot m^{-2}$ or $W \cdot kg^{-1}$). HR was recorded every minute.

During BASE, each subject sat quietly in a semi-recumbent position on a lounge chair for 20 min in 28°C air. Following base, each subject was escorted to the immersion tank to begin the Pre-OCC stage of the water immersion protocol. Each subject sat immersed to the first thoracic vertebrae with limbs separated and extended on a specially designed chair constructed of PVC tubing. Water temperature of the tank was maintained at 20° (± 0.1°C) via a commercially available chiller (Bath Cooler PBC-2II, NESLAB Instrument Company, Newington, NH). After 40 min, or when Tes reached 36.5°C, the OCC stage was initiated. Blood pressure cuffs around the right arm and left leg was inflated to 180 and 220 mmHg, respectively (Glickman-Weiss et al. 2000, Mittleman and Mekjavic 1988). After 10 min of blood occlusion, the cuffs were released and the subject remained in the tank for 10 min for (Post-OCC) or until a Tes of 35°C. Upon release of the cuffs, Tes decreases observed resulting from the return of the cooled extremity blood to the core region and HP concomitantly increases. The slope of the stimulus (decrease in Tes) – response (increase in HP) relationship during the Post-OCC phase was used to define thermosensitivity (β, $W \cdot kg^{-1} \cdot °C$). Following the Post-OCC stage, subjects were removed from the immersion tank and escorted to a warm shower for rewarming.

Statistical Analyses. Data were evaluated for differences between group (YNG vs. OLD) and across time using analysis of variance (ANOVA) procedures. Significance was set *a priori* at $p < 0.05$. When significance was observed, a Tukey post-hoc test was used to examine specific contrasts. *A priori* contrasts on the physiological responses at baseline were compared using a Tukey post-hoc test. All values are expressed as means (M) ± standard deviations (SD). HP was analyzed and is expressed as $W \cdot kg^{-1}$ and $W \cdot m^{-2}$ and ß was analyzed and is reported as both $W \cdot kg^{-1} \cdot °C^{-1}$ and $W \cdot m^{-2} \cdot °C^{-1}$. Both units of measurement are presented so as to make comparisons with the available experimental literature. Lastly, due to the unequal group sizes, Levene's Test for Equality of Variances was used to determine whether group variances were unequal. If the groups exhibited different variances, an adjusted p-value was used.

RESULTS

Physiological Responses During Baseline

There were no significant differences observed in Tes between the OLD vs. YNG (36.8±0.3 vs. 36.2± 0.1 °C, respectively). HP was not significantly different between the OLD and YNG when HP was expressed relative to body weight (1.39± 0.2 vs. 1.32± 0.2 $W \cdot kg^{-1}$, respectively) or A_D (55.3± 5.2 vs. 53.4± 8.1 $W \cdot m^{-2}$, respectively). Tsk also did not differ between OLD vs. YNG (31.2±1.8 vs. 31.7±0.8°C. respectively) during baseline.

Physiological Responses During Cold Water Immersions

Heat production (HP). HP did not demonstrated a main effect for age ($p = 0.190$) when expressing HP in terms of $W \cdot kg^{-1}$ (OLD= 3.18 ± 0.4 vs. YNG= 2.51 ± 0.2 $W \cdot kg^{-1}$), or when expressing HP in $W \cdot m^{-2}$ ($p = 0.147$). A significant main effect for time ($p < 0.001$) was observed when HP was expressed in either $W \cdot kg^{-1}$ or $W \cdot m^{-2}$ whereby HP exhibited a characteristic elevation during the onset of immersion followed by a slight decrease or plateau during the Pre-OCC and OCC stages and then an increase during the Post-OCC stage (Figure 1). Post-hoc analysis revealed significant differences between all time periods except for Pre-OCC and OCC (Table 2).

Insert Table 2, Figure 1

Esophageal temperature (Tes). Tes did not demonstrate a main effect for age ($p = 0.338$) (OLD = 36.6± 0.1 vs. YNG = 36.7± 0.06°C). Also, as expected a significant main effect for time was observed ($p < 0.001$) (Figure 2, Table 2). Post-hoc testing revealed significant differences between BASE and POST-OCC, PRE-OCC and OCC, and, OCC and POST-OCC only (Table 2). Additionally, there was no significant group x time interaction demonstrated.

Insert Figure 2

Mean skin temperature (Tsk). Tsk did not demonstrate a main effect for age ($p = 0.274$) (OLD = 23.8 ± 0.31 vs. YNG = 24.2 ± 0.19°C). Figure 3 displays the response in Tsk over time. As expected, a significant main effect for time ($p < 0.01$) was observed and subsequent post-hoc testing revealed differences between all time points except for pre-OCC and OCC and Post-OCC. (Table 3).

Insert Figure 3

Central Thermosensitivity (ß). The relationship between the decrease in Tes and increase in HP following the release of occlusion and subsequent recirculation of the cooled extremity blood is depicted for all subjects in Figure 4. All values for ß are given as absolutes. As depicted in Figure 4, ß was higher, but not significantly different ($p = 0.10$) in the YNG group than the OLD group (3.56 ± 1.6 vs. 2.25 ± 1.6 $W \cdot kg^{-1} \cdot °C^{-1}$, respectively). When expressed relative to A_D (for experimental comparisons), ß was again not significant between the YNG vs. OLD groups ($p= 0.350$; 121.80±63.4 vs. 91.56± 70.69, respectively).

Insert Figure 4

DISCUSSION

In the present study, thermal and metabolic responses were evaluated during immersion in 20°C water following the alteration in blood circulation (by pressure cuff

occlusion). The experimental manipulation of Tes by pressure cuff occlusion and the subsequent release of the cooled trapped extremity blood, resulted in an increase in shivering thermogenesis and a reduction in Tes. This has been reported previously (Mittleman and Mekjavic 1988,1991). The slope of the Tes-HP relationship during the dynamic POST-OCC phase that defines central thermosensitivity did not significantly differ between OLD vs. YNG. This study clearly extends the work of Mittleman and Mekjavic (1988,1991) however, employing a sample of individuals of different ages. Values for central thermosensitivity in the present investigation were similar to those previously reported by Mittleman et al. (1997) (overall mean ± SD: 3.18 ± 1.67 $W \cdot kg^{-1} \cdot °C^{-1}$; YNG = 3.56 ± 1.5 $W \cdot kg^{-1} \cdot °C^{-1}$; OLD = 2.25 ± 1.7 $W \cdot kg^{-1} \cdot °C^{-1}$). This lack of significant difference may be explained by the large variability in the data, indicating that there is a large amount of inter-individual variation in thermosensitivity. The variability in thermosensitivity was similar to that observed in previous studies (Mittleman and Mekjavic 1991, Glickman-Weiss et al. 2000).

As stated previously, it is well established that a combination of factors such as gender, body composition, morphology, age, aerobic fitness and ethnicity may influence the individual's ability to respond to the stressor of cold (Glickman-Weiss et al. 1991, Glickman-Weiss et al. 1993, Mittleman 1990, Nunneley 1978). The subjects in the present investigation were younger (40-50 yrs old) than other studies that have examined the influence of age on thermoregulation, (i.e., Frank et al. 2000 examined 58-71 yr old subjects; Richardson et al. 1992 examined on average 71 yr old subjects, Falk et al. 1994 examined 46-62 yr old subjects). Therefore, the lack of significance in the present

investigation may be due to the similarity in the age groups. Employing samples that consist of more of a disparity in age may therefore elicit differing results.

In addition, the present investigation did not find a difference between Tes between OLD vs. YNG. This response was unaccompanied by differences in Tsk, HP ($W \cdot m^{-2}$ or $W \cdot kg^{-1}$) and ß. Overall, although not significantly different, HP ($W \cdot kg^{-1}$) was higher in OLD compared to YNG, a finding that differs with the experimental literature (Falk et al. 1994, Richardson et al. 1992, Kenney and Buskirk 1995). Frank et al. (2000) and others (Falk et al. 1994, Richardson et a. 1992) have demonstrated that aging is associated with a reduction in total body oxygen consumption as well as a decrease in vasomotor responsiveness. In contrast, Horvath et al. (1955) examined the responses of elderly subjects to an ambient temperature of 10 °C and found no significant changes in oxygen consumption and heat production as a consequence of being moved from a comfortable to a cold environment.

Body temperature depends on the dynamic balance between heat gained through metabolic heat production and heat lost to the environment. Some of the physiological responses to cold exposure include skin vasoconstriction and shivering (an increase in HP), and an increase in sympathetic nervous system activity. When heat loss exceeds heat gain there is a decline in Tes. Since the YNG group exhibited a similar Tes overall compared to their OLD counterparts, it is likely that this was due to a higher HP in the OLD which may have been due to a reduced vasomotor response. Long term this greater metabolic cost may place a greater thermal strain on the older individual. Richarson et al. (1992) reported that when an individual undergoes indirect cooling it elicits a reflex decrease in cutaneous blood flow, which is more pronounced in the deep vessels than in

the supeficial capillaries all of which is attenuated with advancing age. Similarly Frank et al. (2000) reported both a decrease in vasomotor responsiveness and subjective sensory thermal perception. Therefore, although Frank et al. (2000) reports that both peripheral vasoconstriction and shivering thermogenesis, which are the two primary responses that maintain body temperature during a cold challenge, are less effective in the elderly, the present investigation demonstrated that the OLD group in the present investigation was able to maintain a similar Tes compared to the YNG group most likely due to the higher HP.

A limitation of the present investigation is the small sample size and, therefore, the reduced statistical power inherent in the study. However, the majority of the environmental/hypothermia literature does involve very small sample sizes; therefore, the statistical power of those investigations must be considered as well as the difficulty in obtaining subjects to volunteer to participate in this area of research

The determination of central thermosensitivity allows for the assessment of group differences (YNG vs. OLD) in the physiological responses to a decrease in core temperature regardless of the anthropometrical or morphological differences (Mittleman 1991). Therefore, the determination of central thermosensitivity may reveal whether or not a certain group of individuals is at a marked disadvantage during cold exposure. If a marked disadvantage was observed, this information could lead to alterations in acceptable exposure time, equipment / insulation needs, and in general guidelines set forth to protect the individual from cold related injuries. Based on these data the thermosensitivity of HP during cold water immersion is similar between OLD and YNG.

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FIGURE LEGENDS

Figure 1: Mean values for heat production (M±SD): During baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow in young (YNG) vs. OLD (OLD), ($p = 0.137$).

Figure 2: Mean values for esophageal temperature (M±SD): During baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow in young (YNG) vs. old (OLD), ($p = 0.334$).

Figure 3: Mean values for skin temperature (M±SD): During baseline (BASE), prior to (Pre-OCC), during occlusion (OCC), and following the pressure cuff occlusion (Post-OCC) of the extremity blood flow in young (YNG) vs. OLD (OLD), ($p = 0.479$).

Figure 4: Comparison of values for thermosensitivity (M±SD) between young (YNG) and old (OLD), ($p = 0.180$)

Table 1. Subject characteristics (M ± SD).

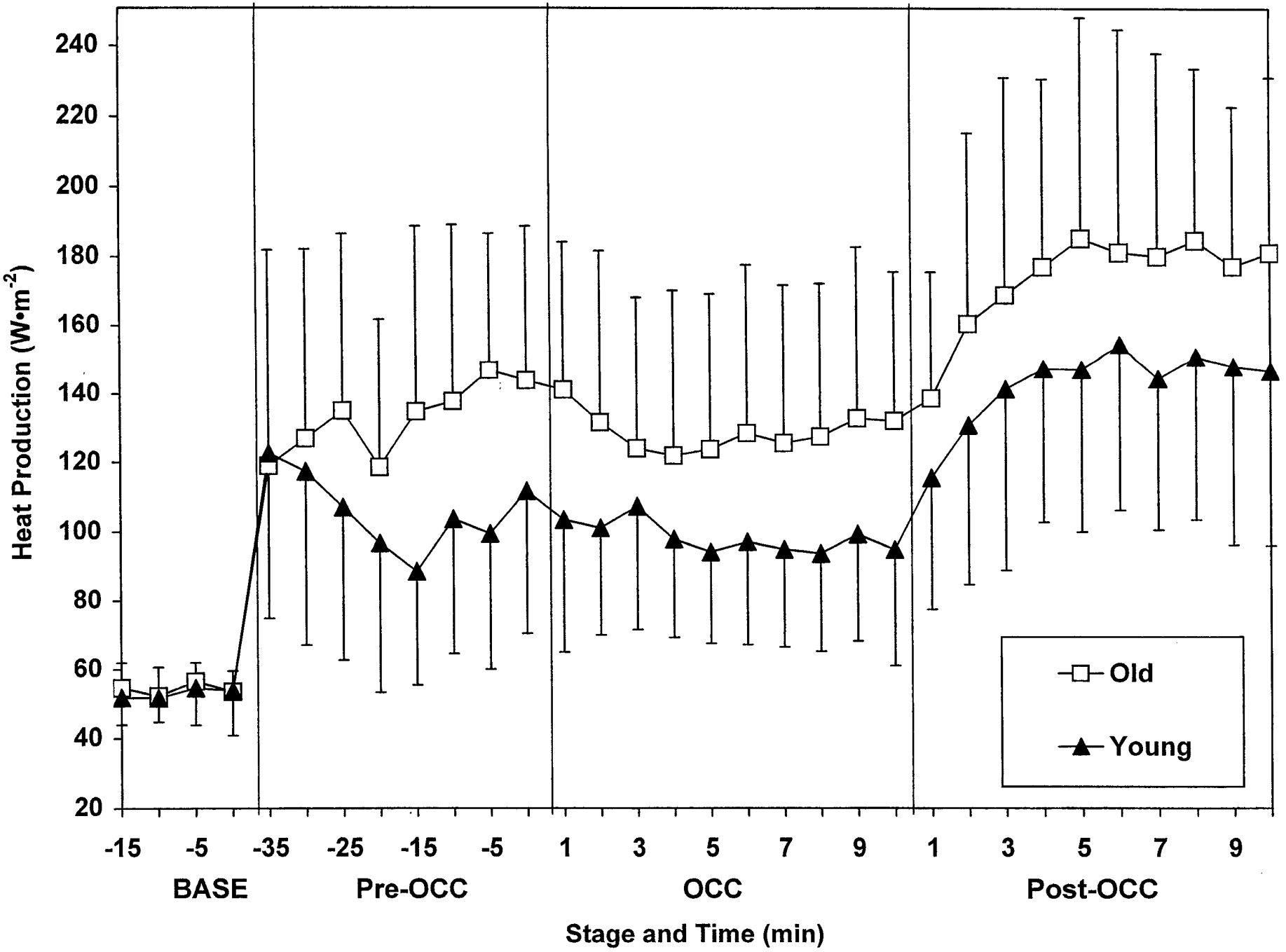
Variable	Young (n=15)	Old (n=5)
Age (yrs)	22.7 ± 2.8	45.2±7.3*
Height (cm)	177.7 ± 7.9	179.7±6.2
Weight (kg)	79.0 ± 11.1	76.2±12.2
BSA (m^2)	1.96 ± 0.2	1.94±0.2
Body fat (%)	10.9 ± 2.9	13.7±8.4
VO_2max ($mL \cdot kg^{-1} \cdot min^{-1}$)	46.4±9.2	43.2±6.5

BSA, Body Surface Area; * $p < 0.05$, young vs. old

Table 2. Esophageal temperature (Tes), mean skin temperature (Tsk), and heat production (HP) across time (M ± SD).

	Tes (°C)			Tsk (°C)			HP ($W \cdot m^{-2}$)		
Stage	**Old**	**Young**	**Total**	**Old**	**Young**	**Total**	**Old**	**Young**	**Total**
BASE	36.8 ± 0.3	37.0 ± 0.2	36.9 ± 0.3	31.2 ±1.9	31.7 ± 0.8	31.6 ± 1.2	55.3 ±5.2	53.4 ± 8.1	53.9 ± 7.4
PRE-OCC	36.7 ± 0.4	36.9 ± 0.2	36.9 ± 0.3	21.5 ±.0.8	22.1 ± 0.9	21.9 ± 0.9	141.2 ±49.8	105.1 ± 49.8	114.1 ± 42.0
OCC	36.6 ± 0.5	36.7 ± 0.2	36.7 ± 0.3	21.4 ±.0.8	21.6 ± 0.9	21.6 ± 0.9	127.5 ±48.0	97.9 ± 28.8	105.3 ± 35.6
POST-OCC	36.3 ± 0.6	36.4 ± 0.3	36.4 ± 0.4	21.2 ±1.0	21.5 ± 0.9	21.5 ± 0.9	167.6 ±56.6	141.7 ± 43.0	148.2 ± 46.5

BASE, Baseline; PRE-OCC, Pre-occlusion; OCC, occlusion; POST-OCC, post-occlusion.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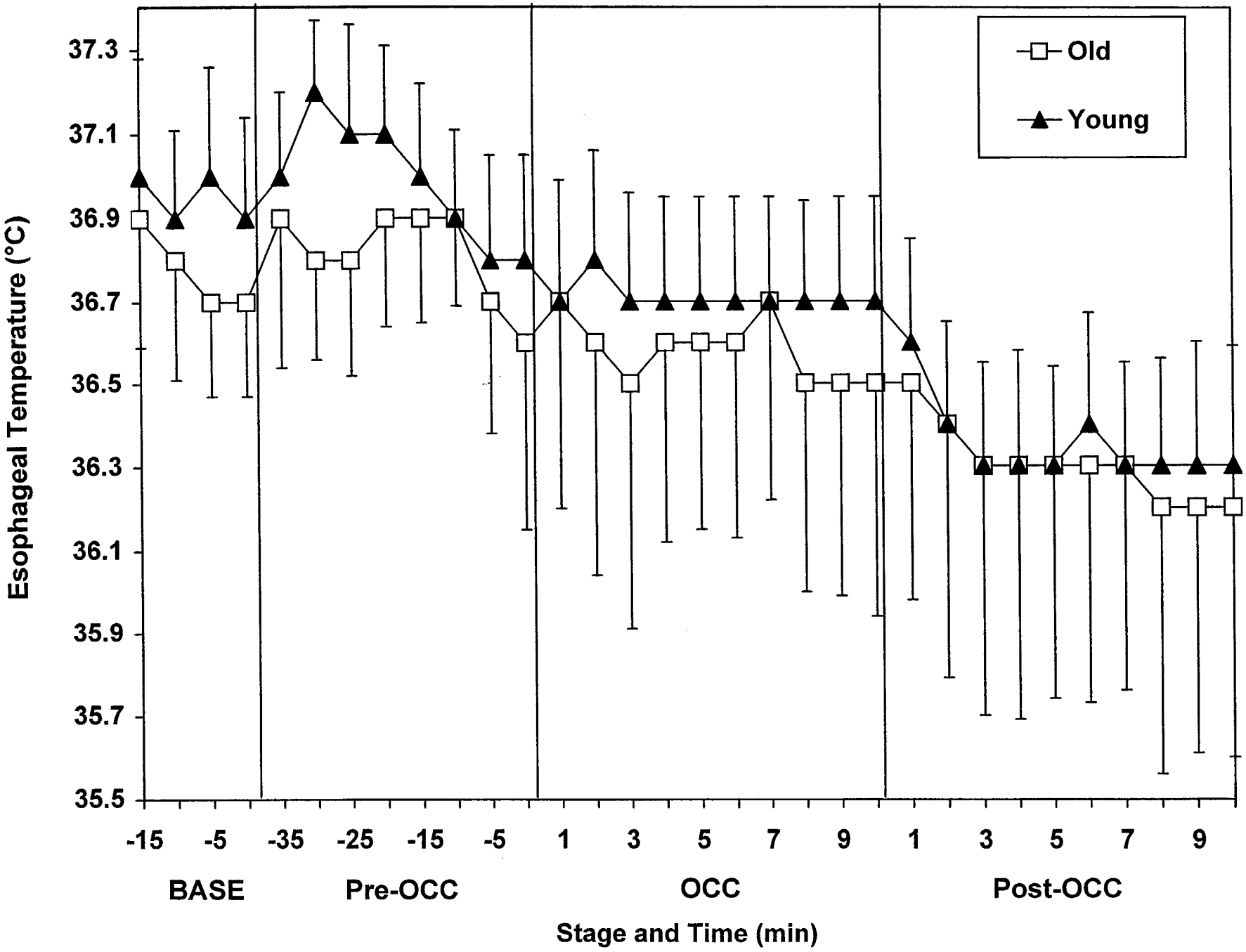
Old
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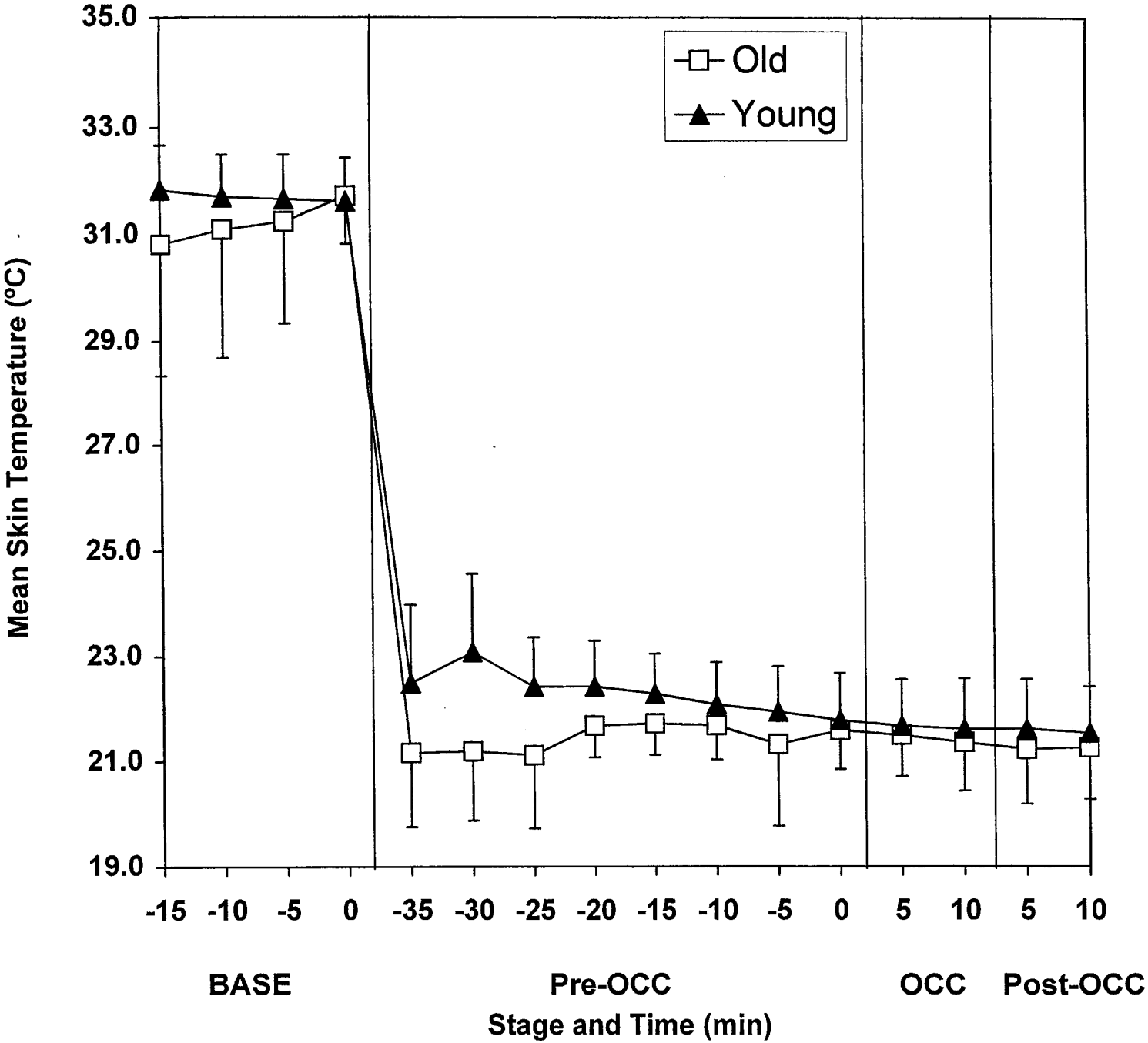
Stage and Time (min)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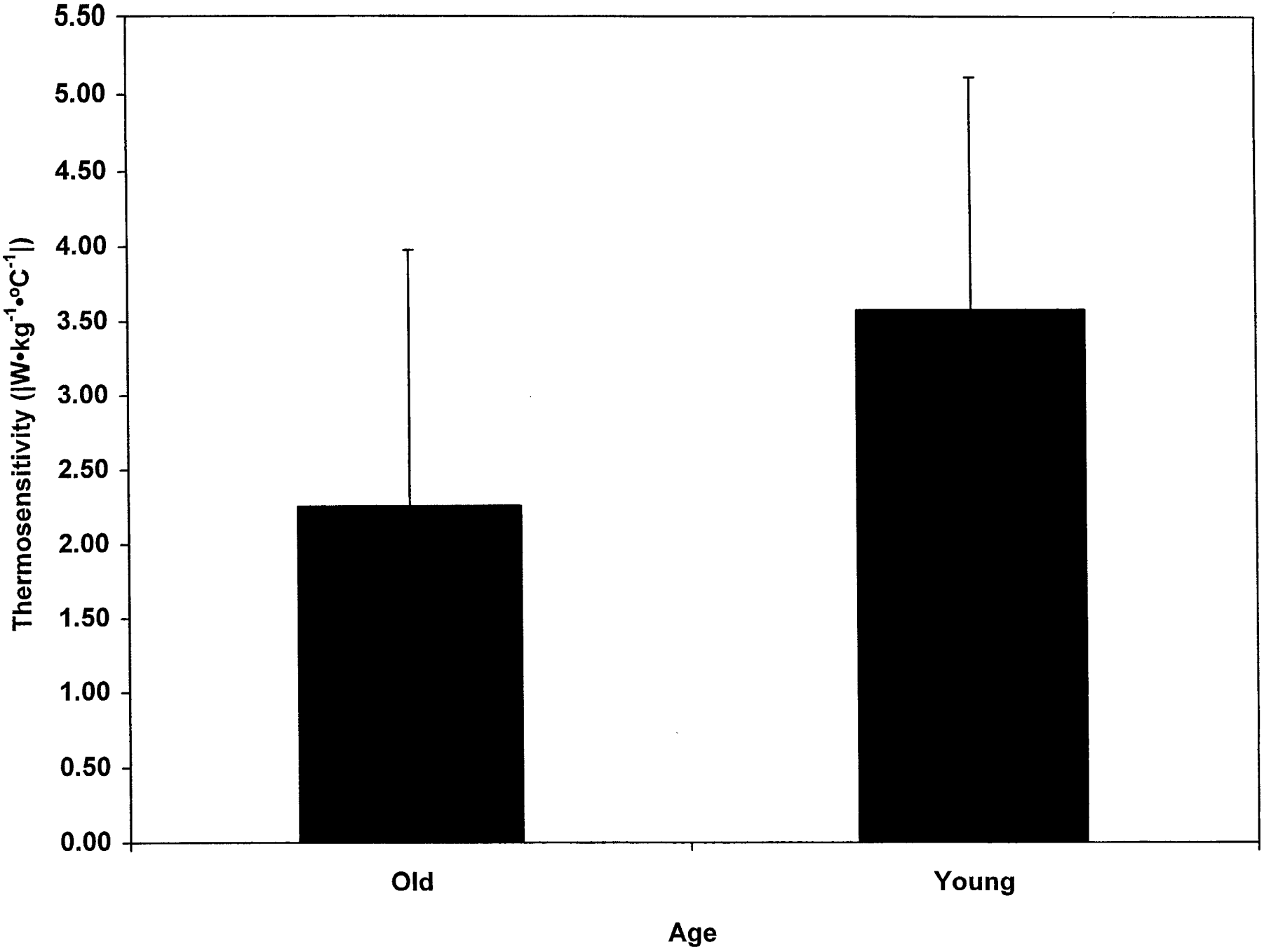
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Thermosensitivity (|W•kg-1•°C-1|)
Old
Young
Age

Appendix E. Abstracts

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THE INFLUENCE OF GENDER AND MENSTRUAL PHASE ON THERMOSENSITIVITY DURING COLD WATER IMMERSION

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(Sponsor: E. Glickman-Weiss, FACSM)

The aim of this investigation was to evaluate the influence of gender and phase of menstrual cycle on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C). Previous research on a limited number of subjects has suggested that thermosensitivity of HP is similar between males and females and is not influenced by menstrual phase. This study re-visited this concept in 10 women (22.4 ± 2.8 yr) during both follicular (FOL: days 1-8) and luteal (LUT: days 19-24) phases and 16 men (22.4 ± 2.9 yr). Following a 20 min baseline period (Base), subjects were immersed to the first thoracic vertebrae until esophageal temperature (Tes) reached 36.5°C or for a maximum pre-occlusion time of 40 min (Pre-OCC). An arm and thigh cuff were then inflated to 180 and 220 mmHg, respectively, for 10 min. Following release of the inflated cuffs (Post-OCC), the slope (ß) of the relationship between the decrease in Tes and the increase in HP was used to quantify thermosensitivity. ANOVA revealed no significant ($p>0.05$) difference between group for Tes, HP and ß ($\bar{X}$ ±SD are reported below).

Variable	Males	Females-FOL	Females-LUT
Base Tes (°C)	37.0 ± 0.30	36.9 ± 0.20	37.0 ± 0.30
Base HP ($W \cdot kg^{-1}$)	1.33 ± 0.16	1.25 ± 0.20	1.26 ± 0.15
Pre-OCC Tes (°C)	36.9 ± 0.20	36.9 ± 0.30	36.7 ± 0.40
Pre- OCC HP ($W \cdot kg^{-1}$)	2.69 ± 0.96	2.13 ± 0.85	2.09 ± 0.71
ß ($W \cdot kg^{-1} \cdot °C$)	-3.24 ± 1.98	-2.76 ± 1.30	-3.05 ± 1.75

These data support the previous findings that the thermosensitivity of HP during cold water immersion is similar between males and females and is not influenced by menstrual cycle phase.

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THE INFLUENCE OF GENDER AND MENSTRUAL CYCLE PHASE ON A COLD AIR TOLERANCE TEST AND ITS RELATIONSHIP TO THERMOSENSITIVITY

E. Glickman-Weiss, FACSM, C. Cheatham, N. Caine, and M. Blegen
K. Mittleman, FACSM. Kent State University, Kent, OH e-mail: wglickma@kent.edu (Sponsor: E. Glickman-Weiss, FACSM)

This investigation evaluated the influence of gender and phase of menstrual cycle [follicular (FOL): days 2-6 and luteal (LUT): days 19-24] on a cold air tolerance test (CATT: 90-min of exposure to 5°C air) in 8 females (22.4 ±2.8 yrs) and 15 males (22.4 ± 2.9 yrs). In addition, central thermosensitivity (ß) [i.e., the slope of the relationship between the decrease in esophageal (Tes) temperature and the increase in heat production (HP)] gathered during a separate water trial in 20°C water, was correlated to the change in Tes and HP across the 90-min of resting exposure during the CATT. ANOVA revealed no significant difference between phase of menstrual cycle or gender between men and women for HP, mean skin temperature (Tsk), and insulation (I), however a main effect for time for these parameters was demonstrated. Despite these similarities, Tes differed ($p<0.05$) between men and women. Additionally, there was no relationship found between ß and ΔHP and ΔTes. These data suggest that menstrual cycle phase did not cause a differential response in Tes, Tsk, I and HP during a CATT. However, women (pooled) maintained a higher ($p<0.05$) Tes than men during the CATT despite similarities in HP and Tsk. Also, there was no relationship between ß (in water) and thermoregulation during the CATT in these subjects.

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THE INFLUENCE OF ETHNICITY ON THERMOSENSITIVITY DURING COLD WATER IMMERSION

E.L.Glickman, FACSM, C.C. Cheatham, N. Caine, and M. Blegen, Kent State University, Kent, OH e-mail: wglickma@kent.edu

The purpose of this investigation was to evaluate the influence of ethnicity, on thermosensitivity and metabolic heat production (HP) during cold water immersion (20°C) in 15 Caucasian [(CAU) 22.7 ± 2.7 yr.] vs. 7 African-American [(AA) 21.7 ± 2.7 yr.] males. Following a 20 min baseline period (BASE), subjects were immersed in 20°C water until esophageal temperature (Tes) reached 36.5°C or for a maximum pre-occlusion (Pre-OCC) time of 40 min. Arm and thigh cuffs were then inflated to 180 and 220 mmHg, respectively, for 10 min (OCC). Following release of the inflated cuffs (Post-OCC), the slope of the relationship between the decrease in Tes and the increase in HP was used to define thermosensitivity (ß). ANOVA revealed no significant difference in thermosensitivity between CAU and AA (CAU = 3.5 ± 1.6 vs. AA = 2.4 ± 1.4 $W \cdot kg^{-1} \cdot °C^{-1}$). No significant differences ($p > 0.05$) were found for Tsk (CAU = 24.3 ± 0.3 vs. AA = 25.1 ± 0.4°C) or HP ($p > 0.05$; CAU = 2.5 ± 0.2 vs. AA = 2.2 ± 0.3 $W \cdot kg^{-1}$). However, a significant ($p < 0.05$) main effect for ethnicity for Tes was observed (CAU = 36.7 ± 0.1 vs. AA = 36.5 ± 0.1°C). These data suggest, despite a differential response in Tes between AA and CAU groups, the ß of HP during cold water immersion is similar between CAU and AA. Therefore, these data demonstrate that when faced with a cold challenge, there is a similar response in HP between CAU and AA that is accompanied by a differential response in Tes.

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Appendix F.

Personnel list that received compensation from this research effort.

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Cheatham CC

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Mittleman KD

Simmons C

Zacher C